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<p>(54) Title: A SYSTEM AND METHOD FOR DETECTING, LOCALIZING, AND CHARACTERIZING OCCLUSIONS AND ANEURYSMS IN A VESSEL</p> <p>(57) Abstract</p> <p>The invention relates to a method, and devices for detection, localization, characterization of occlusions, aneurysms, wall characteristics, and vascular bed. The invention is based on introducing an artificial pressure or flow excitation signal (a single signal or more) into the blood vessel (or in other tubular flowing fluid conduits), measurement, analysis of the pressure, and/or flow. The invention discloses a method, and devices for detection, characterization of partial or total occlusion or aneurysm in blood vessels or in other tubular flowing fluid conduits within a body, such as urine flow in the urethra. A system (1) for carrying out the invention includes a signal conditioner (23) operatively connected to a pressure sensor (4), an analog to digital converter (28) connected to the signal conditioner (23), a computer (25) which processes signals from pressure sensors (24A, 24B), the analog to digital converter (28), and displays data on the display (21).</p>			

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**A SYSTEM AND METHOD FOR DETECTING, LOCALIZING, AND  
CHARACTERIZING OCCLUSIONS AND ANEURYSMS IN A VESSEL**

**FIELD OF THE INVENTION**

- 5 This invention relates to the field of medical interventional diagnostic devices. In particular, this invention provides a system and method for the detection, localization, and characterization of occlusions and aneurysms in blood or other body vessels and to the evaluation of clinical treatment success (e.g. tracking sufficient opening of the occlusion or malpositioning of a stent). Also, this invention provides a method and system for vessel wall 10 characterization and diagnosis of the vascular bed.

**BACKGROUND OF THE INVENTION**

Vascular diseases are often manifested by reduced blood flow due to atherosclerotic occlusion of vessels. For example, occlusion of the coronary arteries supplying blood to the 15 heart muscle is a major cause of heart disease. Invasive procedures for relieving arterial blockage such as bypass surgery and balloon dilatation with a catheter are currently performed relying on estimates of the occlusion characteristics and the blood flow through the occluded artery. These estimates are based on measurements of occlusion size and/or 20 blood flow or blood pressure before and after the stenosis. Unfortunately, current methods of occlusion size and blood flow measurement have low resolution, are inaccurate, are time consuming, require expertise in the interpretation of the results and are expensive. Thus, decisions on whether or not to use any of the blockage relieving methods and which of the 25 methods should be used are often based on partial information. The evaluation of therapeutic success is also problematic, where both occlusion opening and stent position must be evaluated.

Typically, the physician first selects the appropriate treatment method from among 30 medication therapy, transcatheter cardiovascular therapeutics (TCT), coronary artery bypass grafting (CABG), or non-treatment. Atherosclerotic lesions may have different characteristics. Some lesions exhibit a variable degree of calcification while others have a fatty or thrombotic nature. Lesion characteristics together with vessel condition distal to the lesion and the vascular bed (VB) condition are the major factors for determining the

therapeutic procedure needed. Recently, increasing numbers of patients are directed toward TCT. TCT starts with an interventional diagnosis procedure (most commonly used is angiography), followed by the treatment of the patient with medication therapy, CABG or continuation of the TCT procedure with adequate interventional treatment. TCT final stage includes diagnosis tools, for the evaluation of treatment success.

Numerous methods are currently available for treating various lesion types. Some of these methods are given herein below, sequenced from "softer" to "heavier", relating to their ability to open calcified lesions; percutaneous transluminal angioplasty (PTCA), "Cutting balloon" angioplasty, directional coronary atherectomy (DCA), rotational coronary atherectomy (RCA), Ultrasonic breaking catheter angioplasty, transluminal extraction catheter (TEC) atherectomy, Rotablator atherectomy, and excimer laser angioplasty (ELCA). Often, stents are placed within the lesion so as to prevent re-closure of the vessel (also known as recoil). If the stent is malpositioned ,it disrupts the flow and may initiate restenosis.

Lesion characteristics, together with vessel condition proximal and distal to the lesion and vascular bed condition are used to determine the medically and economically optimal treatment method or combination of methods of choice. The main geometrical parameter of the lesion is stenosis severity As/Ao. Here is the minimal open cross-sectional area of the stenosis and A0 is the nominal cross-sectional area of the unobstructed vessel .The second parameter is the stenosis length. Another clinically important lesion characteristic is the lesion calcification level. A non-calcified arterial wall or lesion is usually a non-chronic, fat based plaque that may be treated by medication therapy, or by the softer, less expensive, PTCA method. Heavily calcified lesion typically requires harder methods, such as ELCA .The calcification level influences the decision whether to use a dilatation balloon prior to stenting. For example, in cases of very soft lesions, the physician may elect not to use a dilatation balloon prior to stenting. In cases where the degree of calcification dictates the use of such a balloon, the vessel wall calcification level influences the optimal inflation pressure of the dilatation balloon. Chapter 12 entitled "CALCIFIED LESIONS" of the book "The New Manual of Interventional Cardiology" (Eds. Mark Freed, Cindy

Grines and Robert D. Saffian, Physicians' Press, Birmingham, Michigan, 1996, pp. 251-261), discusses various methods for the assessment of the degree of vessel wall calcification and their importance in selecting a treatment method.

- 5 Decisions about post dilatation processes such as stent deployment for preventing wall recoil and restenosis, or radiation exposure for preventing restenosis caused by cell proliferation, are also influenced by vessel wall and lesion characteristics. Unfortunately, while lesion geometry is evaluated by angiography, qualitative coronary angiography (QCA), or by intravascular ultrasound (IVUS), accurate information regarding the vessel
- 10 wall structure and composition and the degree of calcification of the lesion and of the vessel wall sections neighboring the lesion is frequently unavailable due to the expenses involved in obtaining this information. Angiography has been the main diagnostic tool in the cath lab. The physician interprets angiographical images in the following sequence: identification and location of the severe lesions, evaluation of the occlusion level (in
- 15 diameter percentage of the occluded portion), qualitative estimation of the perfusion according to "thrombolysis in myocardial infarction" (TIMI) grades, determined according to the contrast material appearance. TIMI grades 0,1,2,3 represent no perfusion, minimal perfusion, partial perfusion and complete perfusion, respectively.
- 20 Among the more sophisticated diagnostic tools are qualitative coronary angiography (QCA), intravascular ultrasound (IVUS), intravascular Doppler velocity sensor (IDVS) and intravascular pressure sensor (IPS). QCA calculates geometrical properties from angiographic images, in image zones that are chosen by the physician. IVUS provides accurate geometrical data regarding cross section area and accurate information regarding
- 25 the vessel wall structure and composition. Physiological parameters have been introduced in order to help the clinician to elect the appropriate clinical solution. IDVS provides velocity measurements, enabling discriminating various degrees of occlusion according to coronary flow reserve (CFR) criteria. IDVS suffers from inaccuracy problems resulting from positioning errors within the vessel.
- 30 IPS provides pressure measurements enabling discriminating various degrees of occlusion according to the FFR (fractional flow reserve) criteria and according to the pressure drop

across the stenosis. While measuring the pressure based parameters, the transducer should cross the stenosis and measure pressure downstream of the stenosis. The need to cross the stenosis prevents the use of this parameter for purely diagnostic purposes, since stenosis crossing is considered of high risk and therefore, unjustified for diagnostic purposes.

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Angiography and the sophisticated techniques discussed above may be employed prior to and after therapeutic procedure (the last for the evaluation of the results and decision about correcting actions). Unfortunately, the above discussed sophisticated methods are rarely used due to their high price, operation complexity and the prevailing feeling among 10 physicians that while they provide more accurate information, this information usually does not contribute to clinical decisions.

Pressure, flow and geometry are three variables often measured in the cardiovascular system. Recent progress in invasive probe miniaturization, improvements of the frequency

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response of probe sensors and computerized processing have opened a whole new range of intravascular pressure and flow measurements and analysis that have been previously impossible to perform. A method for determination of the reflection sites in the arterial system was suggested by Pythoud, F. Stergiopoulos, N. Westerhof, N. and Meister, J.J. in "Method for determining distributions of reflection sites in the arterial system" in Am. J.

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Physiol 271 (1996). They studied reflections of pressure and flow waves generated by the beating heart, in the arterial tree using simultaneous pressure and flow measurements. The low (up to 10 Hz) bandwidth of the pressure and flow signals prevents accurate determination of the distance to reflection site by these authors. Correct determination of reflection source location requires accurate estimation of the pressure wave velocity (PWV)

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in the vessels under consideration and under the specific pressure signal, in contrast with literature data that is based on healthy arteries under beating heart pulses. All known methods for PWV measurement, used two, three or more simultaneous measurements, which prove impractical considering clinically available tools and methods. Further, various attempts have been done to analyze pressure and flow wave changes caused by occluded 30 sites. Harmonic distortions, changes in pressure wave velocity phase velocity, wave attenuation, and additional reflection sites within the arterial tree prevent successful

interpretation and implementation within clinical methods or tools.

### SUMMARY OF THE INVENTION

The invention discloses a method and devices for detection, localization and characterization of occlusions, aneurysms, wall characteristics and vascular bed by introducing an artificial pressure or flow excitation signal (a single signal or multiple signals) into the blood vessel (or in any other tubular flowing fluid conduits), measurement and analysis of the pressure and or flow. The invention provides a method and devices for detection and characterization of partial or total occlusion or aneurysm in blood vessels or  
5 in other tubular flowing fluid conduits within a body, such as urine flow in the urethra.  
10

This invention provides a method of determining the geometrical shape of the stenosis. Such determination as provided for herein is determined by comparing the pressure signal proximal to the stenosis to the pressure signal distal to the stenosis so as determine the  
15 geometrical shape of the stenosis. In another embodiment the reflection method as disclosed herein is determined and then based on the reflection the geometrical shape of the stenosis is determined.

This invention provides a method and devices may also serve for evaluating the success of  
20 medical treatment. For example tracking sufficient opening of the occlusion or malpositioning of a stent. It may also serve for the characterization of vascular bed, downstream the vessel.

The present invention includes also a method for further analysis of the response to the  
25 excitation signal yielding a quantitative determination of elastic properties of blood vessel walls for characterizing, *inter alia*, the distensibility and the compliance of lesioned and non-lesioned parts of blood vessels. The derived elastic properties may be further used to determine the degree of calcification of lesioned and non-lesioned parts of blood vessels.

30 This invention provides an apparatus for detecting, locating and characterizing changes in a tubular conduit system within a living body for transferring fluids, said apparatus

comprising: a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said tubular conduit system; a signal sensor operative to receive said probe signal following transmission into said tubular conduit system; a processor unit operatively connected to said signal sensor; a program for controlling the processor unit; said processor unit operative with said program to receive said probe signal following transmission through said tubular conduit system: identify changes in said probe signal; detect characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal; and recognize and assign a label said characteristic of said tubular conduit said system.

This invention provides a processor apparatus for detecting, locating and characterizing changes in a tubular conduit system within a living body for transferring fluids for use with a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said tubular conduit system and a signal sensor operative to receive said probe signal following transmission into said tubular conduit system, said processor apparatus comprising: a processor unit operatively connected to said signal sensor; a program for controlling the processor unit; said processor unit operative with said program to receive said probe signal following transmission through said tubular conduit system: identify changes in said probe signal; detect characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal; recognize and assign a label said characteristic of said tubular conduit said system; and ascertain and assign a value corresponding to the location and size of said characteristic of said tubular conduit.

This invention provides a method for using a computer to detect, locate and characterize changes in a tubular conduit system within a living body for transferring fluids wherein said computer is operatively connected to a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said tubular conduit system and a signal sensor operative to receive said probe signal following transmission into said tubular conduit system, said method comprising the steps of:

receiving said probe signal following transmission through said tubular conduit system; identify changes in said probe signal; detecting characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal; and recognizing and assigning a label said characteristic of said tubular conduit said system.

Lastly, the present invention includes also a method for further analysis of the response to the excitation signal yielding a quantitative determination of elastic properties of blood vessel walls for characterizing, *inter alia*, the distensibility and the compliance of lesioned and non-lesioned parts of blood vessels. The derived elastic properties may be further used to determine the degree of calcification of lesioned and non-lesioned parts of blood vessels.

#### BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be understood and appreciated more fully from the following detailed description taken in conjunction with the appended drawings in which like components are designated by like reference numerals:

Figure 1 is a schematic view of a clinical system used for characterizing lesions, aneurysm or vascular bed in blood vessels, constructed and operative in accordance with a preferred embodiment of this invention.

Figure 2 is a schematic functional block diagram illustrating the details of clinical system 1 of Figure 1.

Figure 3 is schematic cross section illustrating the positioning of the sensors, the pressure signal generator (PSG) and the catheter of the system 1 of Figure 1 within an obstructed blood vessel during the operation of the system.

Figure 4 is a schematic cross section illustrating one embodiment of the PSG unit 5 of Figure 1 which was used in preliminary in-vivo studies.

Figure 5 is a schematic view of an in-vitro system used for characterizing lesions, aneurysm or vascular bed in blood vessels.

Figure 6 is schematic cross section illustrating the in-vitro recirculating system 51 of system 41 of Figure 5.

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Figure 7 is schematic cross section illustrating the positioning of the sensors, the pressure signal generator (PSG) and the catheter of the system 51 of Figure 6 during the operation of the system.

10 Figure 8 is a schematic cross section illustrating one embodiment of the PSG unit 5 of Figure 5 which was used in preliminary in-vitro studies.

Figure 9 is isometric description of the setup used in Method 1 including the PSG unit, the single pressure sensor and the catheter within a blood vessel.

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Figure 10 is isometric description of a pig carotid exposed and partially occluded in an in-vivo study, including the PSG unit and the single pressure sensor.

20 Figure 11 is an isometric description of the setup used in Method 5 including the PSG unit, the two pressure sensors and the catheter within a blood vessel without stenosis.

Figure 12 is a graph describing pressure versus time (no. of samples) in a two pressure sensors measurement in-vitro setup as shown in Figure 11.

25 Figure 13 is an isometric description of the setup used in Method 5 including the PSG unit, the two pressure sensors and the catheter within a stenosed blood vessel.

Figure 14 is a graph describing pressure versus time (no. of samples) in a two pressure sensors measurement in-vitro setup as shown in Figure 13.

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Figure 15 is a graph describing the pressure time derivative versus time (number of samples)

as calculated from the data described in Figure 12.

Figure 16 is a graph describing the pressure time derivative versus time (number of samples) as calculated from the data described in Figure 14.

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Figure 17 is a demonstration of the calculation of the stenosis severity as the area ratio of the two peaks resulting from Procedure 1.

10      Figure 18 is an isometric description of the setup used in Method 4 including the PSG unit, a pressure sensor measuring at two points A and B, and a catheter within a stenosed blood vessel.

Figures 19(a)-19(e) present the result of the analysis which separate the forward and backward signals.

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Figure 20 is schematic cross section illustrating the in-vitro recirculating system 51 of system 41 of Figure 5, with the addition of an ultrasonic flowmeter 65 and a stenosis 55.

20      Figure 21 is a graph describing the flow (ml/min) versus time (no. of samples) measured within the in-vitro system 51 of Figure 6, and with a stenosis at a distance of 95cm.

Figure 22 is a graph describing the flow (ml/min) versus time (no. of samples) measured within the in-vitro system 51 of Figure 6, and with a stenosis at a distance of 50 cm.

25      Figure 23 is a graph of two pressure measurements, demonstrating the calculation of pressure wave velocity using Procedure 3.

30      Figure 24 is a graph of two pressure measurements, using the in-vitro system of Figs. 5-7 and a Bio-Tek pressure calibrator as a pressure generator PSG demonstrating the calculation of pressure wave velocity using Procedure 3.

Figure 25 is a graph describing the pressure as measured in an in-vivo study, in an occluded vessel, after application of an excitation pressure, in a system as described in Fig 10.

Figure 26 is a closed view of the signal presented in Figure 25.

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Figure 27 is the result of Procedure 2 applied to the data presented in Figures. 25 and 26, illustrating the separation into two peaks, for the forward and backward signals.

10 Figure 28 is the result of Procedure 1 applied in a long range case as presented in Method no.2. The upper signal is the analysis result of the measured signal presented in the lower figure.

15 Figures 29(a) - 29(B). Figure 29(a) is a schematic of an impulse generator. The generator could generate pulses with different width from 2 micro sec. To 1.6 sec. And with period (distance between pulses) from 2 micro sec. To 2.3 sec. For better adjustment the width and the period are divided to 6 regions and regulated by 4 separate regulators, 2 for period and 3 for the pulse width. The electric pulse generator work from power supply of 9 V. The standard timer microchip 556. Figure 29 (b) is a schematic showing electric pulse generator connected to external equipment which will transfer the electric impulse to an impulse of flow/pressure.

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Figure 30 schematic showing use of a Bio-Teck apparatus.

25 Figure 31 is a block diagram of a PSG device having a pump with an electromagnetic push/pull mechanism.

Figure 32 is a block diagram of a PSG device having an external electromagnetic hammer operative to punch a full-of-fluid membrane.

30 Figure 33 is a block diagram of a PSG device having two separate membrane volumes, one with high pressure in which an external electromagnetic hammer moves or destroys a

membrane separating the chambers.

Figure 34 is a block diagram of a PSG device having a two way linearly Proportional Flow Control Valve operated by straight DC drive signals.

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Figures 35 the exciter in which two fix linked pressure sensors are used.

10 Figure 36 the simulation was carried out for "sharp" and known signal like the signals created by the exciter is described in Figure 35 which two fix linked pressure sensors are

used.

Figure.37 describes the function  $\bar{E}(\tau)$ .

Figure 38 shows the signals received by the two pressure sensors.

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Figure 39 shows the error function E(t).

Figure 40 illustrating an example of the results of the in-vitro data processing with the reflected signals.

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Figure 41 illustrating an example of the results of the in-vitro data processing with the minimal error function.

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Figure 42 illustrating the test data processing when an excited signal is generated together with pressure wave signals simulating the heart beats. The signal configuration which illustrates the reflections induced by the full stenosis.

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Figure 43 illustrating the test data processing when an excited signal is generated together with pressure wave signals simulating the heart beats. The pressure wave caused by the pump simulating the heart beats with peaks induced by exciter.

Figure 44 shows the excitation signal combined with the pressure wave signal enlarged from Figure. 43.

Figure 45 shows the estimated Error-function E(t).

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### DETAILED DESCRIPTION OF THE INVENTION

The form of the pressure and flow wave changes at different locations along the arterial system. The most obvious reason is reflection of the advancing pulse originating by the heart beat from occlusions. Analysis of the pressure and or flow waveform as demonstrated herein identifies and quantifies abnormalities within arteries, mainly occlusions. Pressure wave velocity has its own clinical value as a measure of distensibility or compliance. Significant changes are observed in the hemodynamic characteristics of blood vessels with aging and/or disease-state such as hypertension and atherosclerosis. The nature of heart beat rather low bandwidth and its heart generated pulse variance complicates PWV calculations.

10 The variability of pulse sources beating heart imposes inherent variance between measurements taken either in different patients and even between measurements taken in the same patient but at different times or even the same patient, same time different artery. Basically, the large arteries dilate and stiffen, the collagen / elastin ratio increases, thus reducing the vessel distensibility. For example, the elastic modulus of the human aorta,

15 more than doubles between the age of 20 and 60 years. The diameter of the human ascending aorta increases by 9% per decade, and the aorta wall thickens to a larger extent, raising the ratio of the vessel wall thickness to the vessel's radius. These processes result in an increased pressure wave velocity (PWV) within the vessel. Calcification of the vessel wall in particular regions causes significant increase in PWV in the calcified region.

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25 Regions where PWV increases and decreases along the blood vessel as demonstrated herein mark the calcified zone boundaries, and the increase in the PWV above a reference value are used for evaluating the compliance and the calcification level. The determined value of the PWV are compared to the average PWV value, predetermined statistically for the same blood vessel in a specific age and gender group to which the current patient belongs by calculating and reporting their ratio. Additionally, the PWV value determined within the

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lesion region may be compared to the PWV value(s) determined within one or more non-lesion regions of the same vessel which serve as an internal reference value, by calculating and reporting the ratio of the above PWV values. These PWV measurements and the reported PWV ratio disclosed hereinabove, are useful in the detection of otherwise  
5 "angiographically occult" diseased vessel regions.

This invention provides an apparatus for detecting, locating and characterizing changes in a tubular conduit system within a living body for transferring fluids, said apparatus comprising: a signal generator configured to transmit into said tubular conduit a probe signal  
10 that changes in response to encountering changes in said tubular conduit system; a signal sensor operative to receive said probe signal following transmission into said tubular conduit system; a processor unit operatively connected to said signal sensor; a program for controlling the processor unit; said processor unit operative with said program to receive  
15 said probe signal following transmission through said tubular conduit system: identify changes in said probe signal; detect characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal; and recognize and assign a label said characteristic of said tubular conduit said system.

20 In one embodiment the pressure signal originates from catheterization laboratory injection system. The signal may be either one of the internally generated waveforms or excited electronically from a separate signal generator either a stand alone unit or integrated within the system computer, otherwise used for data acquisition and analysis. In another embodiment the pressure signal may originate from an impact mechanism system , e.g. a  
25 spring loaded or electronically activated mechanical impact system, applying pressure on either the catheter or on a container attached to it. In one embodiment the processor unit is operative to select a method from a plurality of methods to identify changes in said probe signal and therefrom detect changes in said tubular conduit system. For example, the processor unit is operative to detect aneurysms, stenosis, and/or arterial occlusions.

30 The method is based on introducing an artificial pressure signal into the blood vessel. In one

embodiment the pressure signal originates from a pressure signal generator (PSG). For example, a PSG of the type suitable for this purpose is a "blood pressure systems calibrator" model 601A, commercially available from Bio-Tek Instruments Inc., Highland Park, Box 998, Winooski, VT-05404-0998, U.S.A. Catheterization laboratory injection systems are known to those skilled in the art. For example, a system of the type suitable for this purpose is a "Mark V Plus Injection System" from Medrad, inc. 271 Kappa Drive, Pittsburgh, PA 15238-2870 U.S.A. Other examples include but are not limited to the following: a pressure signal generated within the catheter or in its distal tip (e.g. piezoelectrically or by another form of energy burst introduction e.g. AcolysisSystem, 5 ultrasound thrombolysis selective lysis of fibrin, by Angiosonics Inc., NC, U.S.A.); is by the movement of an hydrodynamic surface, activated either manually or by a special mechanism (e.g. catheter used for removing malpositioned or embolized stents, for example Amplatz Goose Neck Snare GN 500 and Microsnare SK200 from Microvena corporation, Minnesota USA and catheters which prevent plaque debris from moving downstream); a 10 pressure signal caused by an external controlled pressure applied on an organ, transmitted into a pressure signal within the vessel; a pressure signal caused by a non-invasive energy transmission into the vessel (e.g. ultrasound) in which the artificial pressure/flow signal may be either controlled or measured (within the catheter or the vessel).

15 20 In one embodiment the signal generator is a pressure signal generator. As contemplated herein the signal generator is a pressure sensor. In another embodiment the signal generator is a flow signal generator. As contemplated herein the signal generator is a pressure sensor.

In another embodiment the signal generator is a pressure signal generator; said signal sensor 25 is a pressure signal sensor; and said processor unit is operative to receive a heart beat signal; and synchronize receipt of said probe signal with said heart beat signal. As contemplated herein, the signal sensor includes at least two sensing transducers disposed in spaced apart relation. The signal sensor is movable between at least two positions relative to said tubular conduit system and said processor unit is operative to calculate a pressure wave velocity 30 from signals received from said two positions. In another embodiment the signal sensor includes a signal conditioner. The signal may be derived from either one of the internally

generated waveforms or excited electronically from a separate signal generator either a stand alone unit. A stand alone unit is of the type suitable is a multifunction synthesizer model HP8904A from HP Test and measurement Organization, a Hewlett Packard company USA) or integrated within a system computer, otherwise used for data acquisition and analysis. For  
5 example, an electric impulse generator is shown in Figure 29.

In another embodiment the pressure signal may originate from an impact mechanism system. Such impact mechanisms are known to those skilled in the art. For example, the impact mechanisms may be of the spring loaded or electronically activated mechanical  
10 impact system types, applying pressure on either the catheter or on a container attached to it. A signal generation apparatus (in vitro and in vivo) of the impact mechanism type makes use of a pistol hammer mechanism, where the pistol hammer hits directly on the catheter, lying on a rigid surface, as shown in Figure 4. The pistol used was a P230 semiautomatic pistol from Sig Sauer, Switzerland. Alternatively, the same pistol hammer hit the head of  
15 a standard 5 ml syringe, where the syringe was connected to the catheter through a standard manifold, as shown in Figure 8.

The artificial pressure flow signal may also be synchronized with heart beats, either by gating to ECG or to system measurements (pressure or flow) in which the ECG device  
20 measures heart beat signals upon reaching a desired time in the heart beat triggering the artificial pressure flow signal. The pressure signal advances through a catheter lumen into the blood vessel. The catheter may be a guiding catheter. A guiding catheter of the type suitable for this purpose is a 8F Archer coronary guiding catheter from Medtronic Interventional Vascular, Minneapolis, U.S.A.. A diagnostic catheter of the type suitable for  
25 this purpose is a Siteseer diagnostic catheter, from Bard Cardiology. U.S.A. A balloon catheter of the type suitable for this purpose is a Supreme fast exchange PTCA catheter, by Biotronik GMBH & Co, U.S.A. It should be noted that almost type hollow catheter may be used. The presence of occlusion or aneurysm downstream creates reflection of pressure and flow waves. By extracting data of the reflected pressure waves, originated in the occluded  
30 site, the location and degree of occlusion can be determined using signal processing methods.

In another embodiment, an impact value is determined to evaluate the following: 1) pressure wave velocity and compliance through 0.5 - 1 cm; 2) Analysis of coronary vessels including a strong stenosis case; and 3) using the heart pulses one can evaluate PWV and compliance through 2.5 - 3 cm (simultaneously measurement) or 5-6cm (one probe measurement) that may be useful for peripheral vessel research. The estimated value of reflection coefficient may be used only for relative assessment of reflection coefficient associated with stenosis of different strength.

10 The performance of pressure wave velocity and reflection site parameters (position and reflection coefficient) estimation is based on two-point pressure measurement carried out inside of an artery. The pressure is measured either simultaneously by two pressure sensors or in different time by single sensor with some additional synchronization mechanism. In the case of the simultaneously pressure measurement two pressure sensors are placed throw  
15 known distance  $d$ . In the single sensor case the pressure is firstly measured in point  $a$  (upstream) and after that – in point  $b$  (downstream). The distance  $d$  between these points is to be estimated. In fact, PWV and compliance  $C$  evaluation reduce to PW propagation time evaluation  $\Delta t$  :  $PWV \sim 1/\Delta t$  and  $C \sim \Delta t^2$  (assume that PWV is constant). For purpose of a time delay  $\Delta t$  estimation next algorithms were used:

- 20
- Foot-to-Foot algorithm

This algorithm is based on time estimation of a pressure pulse front propagation. In instance, one can measure time delay related to 10% pulse level.

- 25
- Best-Matching algorithm (“least mean square” (LMS) based algorithm)

This algorithm is based on optimal, from LMS point of view, time coincidence of two pressure pulses.

- 30
- Generalized Best-Matching algorithm including stenosis parameters (location and

reflection coefficient) estimation

This algorithm is too based on optimal, from LMS point of view, time coincidence of two derived pulses. These pulses are calculated using the measured pressure pulses. In addition to a time delay evaluation a reflection coefficient and a stenosis location are evaluated as well.

The above algorithms' performance was tested by in-vitro data. Different type of stenosis (ID=1,2,full ; blunt or cone) was exploited for testing purpose. A distance between pressure sensors and a stenosis location were varied too. A probing signal was formed by an exciter ("sharp") or by a pump ("broad"). The acceptable accuracy was defined as 10-15%. All the in-vitro experiments were carried out within a latex tube which PWV is ~ 14 m/sec in.

The summarized in-vitro results are presented in the table:

Synchro-Nization	Accuracy depends on stenosis	Minimal distance until stenosis	Stenosis parameter s evalua-tion	Number of pulses	Minimal measured time	Signal type
Embed-Ded	No	~ 1 cm	Available for stenosis > 40%	5	~ 0.7 msec	Exciter
By FF	Yes	-	Not available	10	~ 2 msec	Pump

15

Additionally, the system can also be adopted for use in other non-biological conduits, having a pulsatile flow within, such as water pipes through which pulsatile flow may be induced for measuring and characterizing internal narrowing due to scale deposits. In

another embodiment said tubular conduit system is a blood vessel system and said processor unit is operative to detect changes in arterial characteristics. In one embodiment the tubular conduit system is a urinary vessel system and said processor unit is operative to detect changes in urinary tract characteristics.

5

In another embodiment the probe signal is a plurality of discrete signals; said processor unit is operative to sample said discrete signals and receive pressure wave velocity data. The processor unit is operative to perform a single pressure function using said discrete signals and said pressure wave velocity data. The processor unit when performing said single

10 pressure function is operative to calculate an allpass value and a cepstrum value from said minimum phase component; separate a regular part and a singular part of said cepstrum value, where said singular part and said regular part form said pressure wave; calculate an exponential function of singular part; evaluate a second peak time delay with respect to a forward found in said pressure signal; evaluate a coefficient by calculation of a second peak  
15 amplitude to determine an arterial characteristic; evaluate a location of said arterial characteristic. The processor unit is operative to receive a forward pressure wave signal from a first transducer and a probe signal represented by a plurality of discrete signals sampled overtime. The processor unit is operative to perform a dual pressure function.

20 This invention provides a method of determining the geometrical shape of the stenosis. Such determination as provided for herein is determined by comparing the pressure signal proximal to the stenosis to the pressure signal distal to the stenosis so as determine the geometrical shape of the stenosis. In another embodiment the reflection method as disclosed herein is determined and then based on the reflection the geometrical shape of the stenosis  
25 is determined.

30 In another embodiment said processor unit when performing said dual pressure function is operative to: calculate an allpass component and cepstrum component of a minimum phase component of said forward pressure wave signal received from said signal sensor; apply an inverse filtering of said forward pressure wave signal; apply smoothing by a B-spline function; detect a forward peak location by a global maximum calculation; receive a

threshold value; detect a second peak location by comparison with said threshold, where said threshold is derived from a forward peak maximum value and minimum size of a characteristic; evaluate a second peak time delay with respect to said forward peak; evaluate a reflection coefficient by calculating a forward and reflected peak area; and evaluate a 5 location of said characteristic. The processor unit is operative to calculate a pressure wave velocity from a pressure wave sensed by said first and second transducers. In another embodiment the processor unit includes an analog to digital convertor. In another embodiment the processor unit is further operative to ascertain and assign a value corresponding to the location and size of said characteristic of said tubular conduit.

10

This invention provides a processor apparatus for detecting, locating and characterizing changes in a tubular conduit system within a living body for transferring fluids for use with a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said tubular conduit system and a signal 15 sensor operative to receive said probe signal following transmission into said tubular conduit system, said processor apparatus comprising: a processor unit operatively connected to said signal sensor; a program for controlling the processor unit; said processor unit operative with said program to receive said probe signal following transmission through said tubular conduit system: identify changes in said probe signal; detect characteristics of said 20 tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal; recognize and assign a label said characteristic of said tubular conduit said system; and ascertain and assign a value corresponding to the location and size of said characteristic of said tubular conduit.

25

In one embodiment the processor unit is operative to select a method from a plurality of methods to identify changes in said probe signal and therefrom detect changes in said tubular conduit system. As contemplated herein, the processor unit is operative to detect aneurysms, stenosis, and/or arterial occlusions. In another embodiment, the tubular conduit system is a blood vessel system and said processor unit is operative to detect changes in 30 arterial characteristics.

In another embodiment, the processor unit is operative to perform a single pressure function using said discrete signals and said pressure wave velocity data. In another embodiment, the processor unit when performing said single pressure function is operative to calculate an allpass value and a cepstrum value from said minimum phase component. In another embodiment, the processor unit when performing said single pressure function is further operative to separate a regular part and a singular part of said cepstrum value, where said singular part and said regular part form said pressure wave. In another embodiment, the processor unit when performing said single pressure function is further operative to calculate an exponential function of singular part. In another embodiment, the processor unit when performing said single pressure function is further operative to evaluate a second peak time delay with respect to a forward found in said pressure signal. The processor unit when performing said single pressure function is further operative to evaluate a coefficient by calculation of a second peak amplitude to determine an arterial characteristic. The processor unit when performing said single pressure function is further operative to evaluate a location of said arterial characteristic.

In another embodiment the signal generator is a pressure signal generator, and said signal sensor is a pressure signal sensor; said processor unit is operative to receive a heart beat signal; and synchronize receipt of said probe signal with said heart beat signal. In another embodiment the probe signal is a plurality of discrete signals; said processor unit is operative to sample said discrete signals and receive pressure wave velocity data. This invention provides a method of determining the geometrical shape of the stenosis. Such determination as provided for herein is determined by comparing the pressure signal proximal to the stenosis to the pressure signal distal to the stenosis so as determine the geometrical shape of the stenosis. In another embodiment the reflection method as disclosed herein is determined and then based on the reflection the geometrical shape of the stenosis is determined.

In one embodiment the signal sensor includes two sensing transducers disposed in spaced apart relation and said processor unit is operative to receive a forward pressure wave signal from a first transducer and a probe signal represented by a plurality of discrete signals

sampled overtime. The processor unit is operative to calculate a pressure wave velocity from a pressure wave sensed by said first and second transducers. The processor unit is operative to perform a dual pressure function. In another embodiment, the signal sensor is movable between at least two positions relative to said tubular conduit system and said processor unit 5 is operative to calculate a pressure wave velocity from signals received from said two positions.

In one embodiment the processor unit when performing said dual pressure function is operative to calculate an allpass component and cepstrum component of a minimum phase 10 component of said forward pressure wave signal received from said signal sensor. In another embodiment, the processor unit when performing said dual pressure function is further operative to apply an inverse filtering of said forward pressure wave signal. The processor unit when performing said dual pressure function is further operative to apply smoothing by a B-spline function. The processor unit when performing said dual pressure function is 15 further operative to detect a forward peak location by a global maximum calculation. The processor unit when performing said dual pressure function is further operative to receive a threshold value. The processor unit when performing said dual pressure function is further operative to detect a second peak location by comparison with said threshold, where said threshold is derived from a forward peak maximum value and minimum size of a 20 characteristic. The processor unit when performing said dual pressure function is further operative to evaluate a second peak time delay with respect to said forward peak. The processor unit when performing said dual pressure function is further operative to evaluate a reflection coefficient by calculating a forward and reflected peak area. The processor unit when performing said dual pressure function is further operative to evaluate a location of 25 said characteristic. The processor unit is operative to calculate a pressure wave velocity from a pressure wave sensed by said first and second transducers.

This invention provides a method for using a computer to detect, locate and characterize changes in a tubular conduit system within a living body for transferring fluids wherein said 30 computer is operatively connected to a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said

tubular conduit system and a signal sensor operative to receive said probe signal following transmission into said tubular conduit system, said method comprising the steps of:  
5 receiving said probe signal following transmission through said tubular conduit system; identify changes in said probe signal; detecting characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in  
said probe signal; and recognizing and assigning a label said characteristic of said tubular conduit said system. In one embodiment the method includes the steps of ascertaining and  
assigning a value corresponding to the location and size of said characteristic of said tubular conduit. The method further includes selecting a process from a plurality of processes  
10 identifying changes in said probe signal and therefrom detecting changes in said tubular conduit system.

In one embodiment the tubular conduit system is a blood vessel system, said method further including detecting changes in arterial characteristics, detecting aneurysms, detecting  
15 stenosis, and/or detecting arterial occlusions.

In one embodiment the signal generator is a pressure signal generator, and said signal sensor is a pressure signal sensor; said method including receiving a heart beat signal; and synchronizing receipt of said probe signal with said heart beat signal. In another  
20 embodiment, the probe signal is a plurality of discrete signals; said method including sampling said discrete signals and receiving pressure wave velocity data. The method may include the steps of performing a single pressure function using said discrete signals and said pressure wave velocity data. Performing step includes the step of calculating an allpass value and a cepstrum value from said minimum phase component. Further, performing step  
25 includes the step of separating a regular part and a singular part of said cepstrum value, where said singular part and said regular part form said pressure wave. The step of calculating an exponential function of singular part. In another embodiment, the performing step includes the step of evaluating a second peak time delay with respect to a forward found in said pressure signal. In another embodiment the performing step includes the step of evaluating a coefficient by calculation of a second peak amplitude to determine an arterial  
30 characteristic. In another embodiment the performing step includes the step of evaluating

a location of said arterial characteristic.

In one embodiment the signal sensor includes two sensing transducers disposed in spaced apart relation, said method includes the step of receiving a forward pressure wave signal from a first transducer and a probe signal represented by a plurality of discrete signals sampled overtime. In another embodiment the method further includes the step of calculating a pressure wave velocity from a pressure wave sensed by said first and second transducers. A dual pressure function may be performed. In another the signal sensor is movable between at least two positions relative to said tubular conduit system, said method including the step of calculating a pressure wave velocity from signals received from said two positions.

In another embodiment, the performing step includes the step of calculating an allpass component and cepstrum component of a minimum phase component of said forward pressure wave signal received from said signal sensor. In another embodiment the performing step includes the step of applying an inverse filtering of said forward pressure wave signal. In another embodiment, the performing step includes the step of applying smoothing by a B-spline function. In another embodiment the performing step includes the step of detecting a forward peak location by a global maximum calculation. In another embodiment the performing step includes the step of receiving a threshold value. In another embodiment the performing step includes the step of detecting a second peak location by comparison with said threshold, where said threshold is derived from a forward peak maximum value and minimum size of a characteristic. In another embodiment the performing step includes the step of evaluating a second peak time delay with respect to said forward peak. In another embodiment the performing step includes the step of evaluating a reflection coefficient by calculating a forward and reflected peak area. In another embodiment the performing step includes the step of evaluating a location of said characteristic. In another embodiment the performing step includes the step of calculating a pressure wave velocity from a pressure wave sensed by said first and second transducers.

30

With reference to the Figures for purposes of illustration, reference is now made to Figs. 1

and 2. Figure 1 is a schematic isometric view of a system for characterizing blood vessel occlusions, vascular bed and blood vessel walls constructed and operative in accordance with one embodiment of the present invention. Figure 2 is a schematic functional block diagram illustrating the details of the system 1 of Figure 1.

5

The system 1 includes a signal conditioner 23, such as a model TCB-500 control unit commercially available from Millar Instruments, or Radi Pressure Wire Interface Type PWI10, Radi Medical Systems, Upsala, or other suitable signal conditioner. The signal conditioner 23 is operatively connected to the pressure sensor 4 for amplifying the signals of the pressure sensor. The system 1 further includes an analog to digital (A/D) converter 28 connected to the signal conditioner 23 for receiving the conditioned analog signals therefrom. The system 1 also includes a signal analyzer 20 connected to the A/D converter 28 for receiving the digitized conditioned pressure signals from the A/D converter 28. The signal analyzer 20 includes a computer 25, and optionally a display 21 connected to the computer 25 for displaying text numbers and graphs representing the results of the calculations performed by the computer 25 and a printer 26 operatively connected to the computer 25 for providing hard copy of the results for documentation and archiving. The A/D converter 28 can be a separate unit or can be integrated in a data acquisition computer card installed in the computer 25 (not shown). The computer 25 processes the pressure data which is sensed by the pressure sensors 24A and 24B and acquired by the A/D converter 28 or the data acquisition card (not shown) and generates textual, numerical and/or graphic data that is displayed on the display 21.

Another embodiment of the system 1 is a single unit containing both PSG and data acquisition , analysis and display, with or without correlation to ECG input. The system 1 includes a pressure catheter (or a pressure guidewire) 2 having a pressure sensor 4 attached thereto for measuring the pressure inside a blood vessel. In an exemplary embodiment, the pressure catheter 2 can be the 3F "one pressure sensor" model SPC-330A commercially available from Millar Instruments Inc., TX, U.S.A., or any other pressure catheter suitable for diagnostic or combined diagnostic / treatment purposes such as the 0.014 " guidewire mounted pressure sensor product number 12000 from Radi Medical Systems, Upsala,

Sweden, or Cardiometrics WaveWire pressure guidewire from Cardiometrics Inc. an Endsonics company of CA, U.S.A.

Reference is now made to Figure 3. Figure 3 is a schematic cross section illustrating the 5 positioning of the guiding or diagnostic catheter 3 through which the pressure signal travels, relative to an obstruction and vascular bed within an occluded blood vessel during operation of the system 1 of Figure 1.

The guiding catheter (or diagnostic catheter) 3 together with the pressure catheter or 10 guidewire 2, to which the pressure sensor 4 is attached, are inserted into the vascular system of the patient using a standard connector 8 and standard methods and moved to reach the blood vessel of interest. Figure 3 illustrates a cross section of an artery 30 having an arterial wall 32. The artery 30 also includes a stenotic obstruction 34 obstructing the blood flow through the artery 30. The degree of obstruction is defined as the ratio of the cross-sectional area of the stenotic region to the cross-sectional area of the unobstructed artery (not shown).

15 The cross-sectional area of the stenotic region is the cross-sectional open area at the narrowest part of the occlusion. The obstruction distance is defined as the distance between

the measuring point of the pressure sensor 4 to the narrowest cross-section of the obstruction (not shown). In some of the methods presented below, two pressure measurements are 20 required. In those cases, the proximal measurement may be collected using a pressure transducer 7 (e.g. Baxter Model PX272, pressure monitoring kit from Baxter Healthcare Corporation, Ca, U.S.A.), connected to the guiding catheter of system 1 via the connector 8, or a second intravascular pressure transducer, or the two single pressure sensors may be mounted on a mutual wire or catheter (e.g. Millar 2.5F dual sensor model SPC-721, Millar

25 Instruments Inc., TX, U.S.A.).

The pressure catheter 2 is advanced within the artery 30 proximal to the obstruction 34 in the direction of the arterial blood flow indicated by the arrow labeled 36, or opposite. PSG 30 creates a pressure signal, either synchronized with natural beats (ECG) or not, represented by the arrow 39 labeled  $P_L$ .  $P_M(t)$  is the combination of the incident pressure wave, and the reflected pressure wave  $P_R$  (pressure signal reflected by the stenosis 34), represented by the

arrow 40 labeled  $P_R$ , which was reflected from the obstruction at a time ( $t - t'$ ), wherein  $t$  is the delay time between the forward pressure wave and the reflected pressure wave, read by the transducer. Following, several methods will be presented, serving for distinguishing  $P_I$  from  $P_R$  while measuring  $P_M(t)$ , calculating  $t$  and while knowing PWV determining distance to the reflecting site (either stenosis or VB or both). Several methods for calculating the location and reflection coefficient  $R_F$  of the stenosis are presented. Several methods for calculating the pressure wave velocity are presented. The main geometrical parameter of a stenosis is stenosis severity  $A_s / A_o$ . Here  $A_s$  is the minimum open cross-sectional area of the stenosis and  $A_o$  is the nominal cross-sectional area of the unobstructed vessel. In one model for pressure drop across stenosis, suggested by Young and Tsai (Young D.F. and Tsai F. Flow characteristics in model of arterial stenoseses -II. Unsteady flow. J.Biomechanics 6, 547 - 559, 1973.), allows to relate reflection coefficient to geometrical parameters of the stenosis, characteristics of the excited pressure wave and input impedance of the blood vessel. The related equations may be found in the work N.Stergiopoulos, M. Spiridon, F. Pythoud, J.J. Meister. On the wave transmission and reflection properties of the stenosis. J.Biomechanics, v.29, No.1, pp. 31-38, 1996. In the general case, stenosis severity  $A_s / A_o$  and stenosis length  $L$  may be found only if reflection coefficient is known for different frequencies. Therefore, in the general case the reflection of the exciting pressure signal containing different frequencies must be measured. Another possible way is to determine one of the geometrical parameters (stenosis length or stenosis severity) from QCA. The other parameter may be calculated from the measured reflection coefficient.

For short lesions the reflection coefficient is directly related to stenosis severity and the pressure excitation signal. The same principle holds for flow and velocity measurements. A good approximation of the reflection coefficient, based on the linearized flow theory is given by the following relation:  $R_F = (A_o - A_s) / (A_o + A_s)$ . This relationship holds for short distances where signal attenuation is not significant. For long range stenoses the calculation should correct for the attenuation of the pressure excitation signal and its reflections.

30

The present invention discloses a device and a method for a quantitative determination of

the elastic properties of blood vessels for characterizing, *inter alia*, the real part of the complex Young modulus, the distensibility and the compliance of lesioned and non-lesioned parts of blood vessels. The derived elastic properties may be further used to determine the degree of calcification of lesioned and non-lesioned parts of blood vessels. These parameter values can be calculated and reported in absolute terms as a ratio of the relevant parameter value in the lesion region to the parameter value in a non-lesion region of the same patient. Alternatively, the system may calculate and report a ratio of the relevant parameter determined in the lesion region of the patient to a "standard" average value of the relevant parameter as measured in a group of healthy people with similar physiology (age group, gender, vessel type, etc.). In the second alternative, the system will include means for storing such standard average values of the relevant parameters such as a data-base stored in a suitable storage device included in the system (not shown).

The determination of the elastic properties of an artery is based on calculating the phase velocity of the pressure wave. Reference is now made to Figs. 5-7. Figure 5 is a schematic diagram representing an in-vitro experimental apparatus constructed and operative for determining flow characteristics in simulated non lesioned and lesioned blood vessels, in accordance with an embodiment of the present invention. Figure 2 is a schematic functional block diagram illustrating the functional details of a system including the apparatus of Figure 5 and apparatus for data acquisition, analysis and display.

Reference is now made to Figure 5. The system 41 includes the system 51. The system 41 also includes a signal conditioner 23. A conditioner of the type suitable for this purpose is a model TCB-500 control unit commercially available from Millar Instruments, or any other suitable signal conditioner. The signal conditioner 23 is operatively connected to the pressure sensors 24A and 24B for amplifying the signals of the pressure sensors 24A and 24B. The system 41 further includes an analog to digital (A/D) converter 28 connected to the signal conditioner 23 for receiving the conditioned analog signals therefrom. The system 41 also includes a signal analyzer 20 connected to the A/D converter 28 for receiving the digitized conditioned pressure signals from the A/D converter 28. The signal analyzer 20 includes a computer 25, a display 21 connected to the computer 25 for displaying text

numbers and graphs representing the results of the calculations performed by the computer 25 and a printer 26 operatively connected to the computer 25 for providing hard copy of the results for documentation and archiving. The A/D converter 28 can be a separate unit or can be integrated in a data acquisition computer card installed in the computer 25 (not shown).

- 5      The computer 25 processes the pressure data which is sensed by the pressure sensors 24A and 24B and acquired by the A/D converter 28 or the data acquisition card (not shown) and generates textual, numerical and graphic data that is displayed on the display 21.

The fluidics system 51 of Figure 6 is a recirculating system for providing pulsatile flow.

- 10     The system 51 includes a pulsatile pump 42. A pump of the type suitable for this purpose is a model 1421A pulsatile blood pump, commercially available from Harvard Apparatus, Inc., Ma, U.S.A., however other suitable pulsatile pumps can be used. The pump 42 allows control over rate, stroke volume and systole/diastole ratio. The pump 42 recirculates distilled water from a water reservoir 15 to a water reservoir 14.

- 15     The system 51 further includes a flexible tube 43 immersed in a water bath 44, to compensate for gravitational effects. The flexible tube 43 is made from Latex and has a length of 120 cm. The flexible tube 43 simulates an artery. The flexible tube 43 is connected to the pulsatile pump 42 and to other system components by Teflon tubes. All the tubes in system 51 have 4 mm internal diameter. A bypass tube 45 allows flow control in the system and simulates flow partition between blood vessels. A Windkessel compliance chamber 46 is located proximal to the flexible tube 43 to control the pressure signal characteristics. A Windkessel compliance chamber 47 and a flow control valve 48 are located distal to flexible tube 43 to simulate the impedance of the vascular bed. The system 51 of Figure 5 further includes an artificial stenosis made of a artificial stenosis section 55, inserted within the flexible tube 43. The tube section 55 is made from a piece of Teflon tubing. The internal diameter 52 (not shown) of the artificial stenosis 55 may be varied by using artificial stenosis sections fabricated separately and having various internal diameter. The external diameter of all the artificial stenosis section 55 is 4 mm. Thus, various degree of cross sectional area reduction (40%- 95%) can be generated in the distal part of the flexible tube 43, for simulating various degrees of stenosis.

Reference is now made to Figure 7, which is a schematic cross sectional view illustrating a part of the fluidics system 51 in detail. Pressure is measured along the flexible tube 43 using a pressure measurement system including MIKRO-TIP pressure catheters 58 and 59, such as the model SPR-524 pressure catheter, connected to a model TCB-500 control unit, both commercially available from Millar Instruments Inc., TX, U.S.A.. The catheters 58 and 59 are inserted into the flexible tube 43 via the connector 10, connected at the end of the flexible tube 43. The catheters 58 and 59 include pressure sensors 24A and 24B, respectively, for pressure measurements. It is noted that, other catheters or guide wires made by different manufacturers may also be used, such as various pressure measurement guide wires of the type commercially available from Radi Medical Systems AB, Upsala, Sweden, or from Cardiometrics, an Endosonics company of CA, U.S.A.

The end of catheter 3 is inserted into the flexible tube 43 via a connector 9. The other end is connected to a pressure signal generator unit 5, which creates pressure impulse. The pressure wave advance in the fluid through the catheter 56 to vessel 43. When the pressure wave reaches the artificial stenosis 55, reflection of the pressure wave is created. The pressure sensors 24A, 24B measure the original pressure wave and the reflections from the artificial stenosis, and other reflections of the system such as the reflection from the right flexible tube edge 57. A fluid filled pressure transducer 7 is connected to the system 51 via the connector 9, when additional pressure readings are needed, or in place of a second intravascular pressure transducer, when two pressure measurements are of interest.

The system 51 of Figure 6 also includes a flowmeter 11 connected distal to the flexible tube 43 and a flow meter 12 connected to the bypass tube 45. The flowmeters 11 and 12 are operatively connected to the A/D converter 28. The flowmeters 11 and 12 are model 111 turbine flow meters of the type commercially available from McMillan Company, TX, U.S.A.. However, other commercial available flow sensors may be used.

### EXPERIMENTAL DETAILS SECTION

#### Data acquisition and analysis:

5 Data acquisition was performed using a PC (Pentium 586) with an E series multifunction I/O board 28 model PC-MIO-16E-4 of the type commercially available from National Instruments Inc., TX, U.S.A. The I/O board was controlled by a Labview graphical programming software, commercially available from National Instruments Inc., TX, U.S.A. 10 sec interval of pressure and flow data were sampled at 5000Hz, displayed during the  
10 experiments on the monitor and stored on hard disk. Analysis was performed offline using Matlab version 5 software, commercially available from The MathWorks, Inc., MA, U.S.A.

#### System Implementation Methods and Procedures:

The system uses various methods to detect the existence, location and severity of a stenosis  
15 or aneurysm in a blood vessel. The methods are based on four main data analysis procedures which are described hereinbelow. Other data analysis procedures may be developed based on the principles hereinbelow presented. The choice between procedures depends on the signal length and distance from the lesioned area. These two parameters define the time  
20 of the reflection within the signal; the amount of separation between the forward and backward signal serves to select the proper procedure. In the data presented hereinbelow, acquired on the in-vitro system presented in Figs. 4-6, and with pressure wave velocity of 14 m/sec, three different cases were defined: far distance (over 40 cm), mid distance (10-40 cm) and short distance (2-10 cm) stenoses. Usually, far and mid distance stenoses were found using the Procedure 1 presented below. Short distance stenosis were identified using  
25 both Procedure 1 and 2 presented below.

### **Procedure 1: The dual pressure function**

The following procedure analyzed a downstream pressure measurement, composed of both forward and reflected waves, by a priori knowledge of the forward wave. It was determined from:

- 5 a. an upstream measurement, either simultaneously (additional transducer) or non simultaneously [moving the transducer] or  
b. From a priori knowledge of forward pressure wave , resulting from known pressure excitation with known catheter

- #### **10    Input data required for the procedure:**

1. The forward pressure wave,  $w[n]$ .
  2. The pressure measured by a downstream sensor -  $s[n]$ ,  $n=1, \dots, N$ , where  $N$  is the number of samples.

- ## 15 Assumptions:

1. All measured signals are discrete-time signals.
  2. The vessel is a linear, stable and time-invariant causal system.
  3. The time resolution of the linear system is much less than the time delay of the reflected pressure wave.

- #### 20 4 Reflection coefficient is a constant

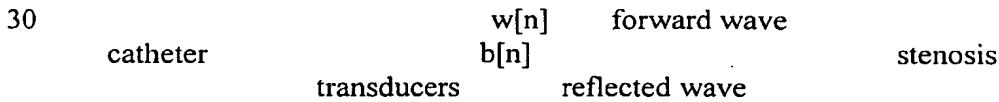
5. Exciting signal (forward pressure wave) is known

6. The pressure wave velocity  $V$  is known. The pressure wave velocity may be calculated with Procedure 3, or assumed to be known from previous test data. It also was known from anatomic data, according to exact vessel, age and clinical situation.

- 25 situation.

#### Experiment setup:

d (cm)



- ### 35 Procedure description:

The following relationship holds:

$$s[n] = w[n] + b[n - m] = w[n] \otimes (\delta[n] + r * g[n-m]); \quad (1)$$

where,

$\otimes$  - is the discrete convolution operator;

40  $s[n]$ - is the measured pressure wave;

$w/n$  - is the forward pressure wave;

$b[n] = r * g[n] \otimes w[n]$  - is the reflected pressure wave;

*d* - is the distance between the downstream sensor to the stenosis;

$g[n]$  - is the response of the vessel in 2d length (to the stenosis and back);

45  $r$  - is the reflection coefficient;

$m = \text{round}(2 * d/v)$  - is the time delay (in samples) of the reflected pressure wave:

$v$  - is the pressure wave velocity;

$\Delta$  - is the distance between transducers.

Using the commutative property of the convolution, Equation (1) describes a digital linear filter:

$$\frac{\delta[n] + r * g[n-m]}{w[n]} \quad w[n] \quad s[n]$$

5 where  $w[n]$  represents the impulse response of this filter.

The parameters  $r$  and  $m$  of the reflected wave describe the stenosis size and location. Therefore, in order to evaluate the stenosis we need to evaluate the reflected wave parameters. In the common case, it is impossible to detect the reflected wave and evaluate 10 its parameters by inspecting the signal  $s[n]$ . In order to get information about the reflected wave inverse filtering to the measured pressure wave was applied:  $\delta[n] + r * g[n-m] = w^{-1}[n] \otimes s[n]$ .

15 The result is a function including two peaks representing the forward and reflected pressure wave and having different amplitudes. The first maximum is equal to 1 and the second one is  $r$ . The time difference between the peaks is the reflected pressure wave delay.

20 As the output signal  $s[n]$  includes measurement noise, smoothing filter  $h[n]$  should be applied prior to the inverse filtration:

$$h[n] \otimes (w^{-1}[n] \otimes w[n]) = h[n] \otimes (\delta[n] + r * g[n-m]) = h[n] + r * (h[n] \otimes g[n-m])$$

Since it was assumed that  $w[n]$  is known, the Minimum-Phase / Allpass decomposition was obtained by iterative procedure described by Tarasov R.P. (Comput.Maths.Math.Phys.,

25 Vol.32,No.10,pp.1373-1390,1992), The computation of functions in the algebra of formal polynomials and multidimensional digital signal processing procedures.

$$w[n] = u[n] \otimes \exp(k[n]), \text{ where}$$

$u[n]$  - is the Allpass component;

$\exp(k[n])$  - is the Minimum-Phase component;

30  $k[n]$  - is the cepstrum of a Minimum-Phase component.

Once  $u[n]$  and  $k[n]$  are evaluated, the inverse filter of the measured pressure wave  $s[n]$  is  $h[n]$ :

$$h[n] + r * (h[n] \otimes g[n-m]) = h[n] \otimes (u[-n] \otimes \exp(-k[n]) \otimes s[n]) \quad (2).$$

35 For final smoothing purpose B-spline was used.

#### Procedure steps:

Step 1: Input :  $w[n]$ . The allpass component  $u[n]$  and the cepstrum  $k[n]$  of the minimum-phase component of the forward wave  $w[n]$  was calculated.

40 Step 2: inverse filtering by expression (2) was applied

Step 3: smoothing by B-spline was applied

Step 4: the forward peak location by global maximum calculation was detected

Step 5: the reflected peak location was detected by comparison with the threshold that depends on forward peak maximum  $M_f$  and minimum stenosis size of interest.

45 Step 6: the reflected peak time delay was evaluated with respect to forward peak by reflected peak shift  $m$  calculation:  $\tau = m * f$ , where  $f$  is the sampling

frequency

Step 7: the reflection coefficient  $r$  was evaluated by calculating the forward and the reflected peak area. Reference is now made to Figure 17. Figure 17 presents the result of Procedure 1, where the first peak represents the input pressure pulse and the second peak represents the reflected pressure wave. The ratio of the area under those peaks serves to estimate the severity of the stenosis or aneurysm, according to the definition presented hereinabove.

5 Step 8: the stenosis location was evaluated by:  $d = v * \tau / 2$

- 10 In the above procedure,  $s(n)$  represents a pressure measurement at point B, as demonstrated in Figure 11.  $W(n)$  was derived as:
1. A second pressure measurement, derived by a second pressure sensor, located upstream at location A - presented in Method 6.
  2. A second pressure measurement derived with the same pressure sensor, moved to an upstream location, designated A - presented in Method 4.
  - 15 3. A prior knowledge of the input signal (excitation signal and transfer function of the catheter) - presented in Method 3.
  4. The initial part (in the time domain) of the pressure signal,  $s(n)$ , for a long range stenosis, where a complete separation of the forward and backward signals occurs - presented in Method 2.

## Procedure 2 : Single pressure function

### Input data required for the procedure:

- 25 1. Pressure versus time function  $Pa[n] = Pa(\Delta t * n)$ ,  $n = 1, \dots, N$ ,  $\frac{1}{\Delta t}$  is the sampling frequency.
- 30 2. Pressure wave velocity. The velocity was assumed to be known from previous test data, or derived according to Procedure 4, presented below.

### Procedure description:

If the exciting signal was unknown, the reflected wave parameters were evaluated by separating the regular  $1n w[n]$  and the singular part  $p[n]$  of the  $1n s[n]$  where

35  $1ns[n] \approx k_s \approx 1n w[n] + p[n]$  and  $1nw[n] \approx k[n]$ .

40 
$$p[n] = \sum_{i=1}^j (-1)^{i+1} r^i * \delta^i[n-i*m]/i, \delta^{i-1}[n] = \delta[n] \otimes \delta[n-m], \delta^0[n] \equiv \delta[n].$$

where

$s[n] = w[n] + b[n-m] = w[n] \otimes (\delta[n] + r * g[n-m])$  is the measured pressure wave;

### Procedure steps:

45 Step 1: the allpass component  $u_s[n]$  and the cepstrum  $k_s[n]$  of the minimum-phase

component:  $s[n] = u_s[n] \otimes \exp(k_s[n])$  was calculated.

Step 2: the regular  $l_{nw}[n]$  and the singular  $p[n]$  part of the  $k_s[n]$  were separated

Step 3: the exponential function of the  $p[n]$ :  $q[n] = \exp p[n]$  was calculated

Step 4: the reflected (second) peak time delay  $\tau$  with respect to forward peak:  $\tau = m * f$

5 , where  $f$  - is the sampling frequency was evaluated

Step 5: the reflection coefficient  $r$  by calculation of the reflected amplitude, or area  
(as demonstrated in Figure 17) was evaluated.

Step 6: the stenosis location by:  $d = v * \tau / 2$  was evaluated

**Procedure 3: Pressure wave velocity with two pressure transducers.**

Simultaneous pressure measurements with two pressure transducers was determined as follows: the pressure wave velocity was derived as  $DL/Dt$ , where  $DL$  is the distance between the transducers and  $Dt$  is the time delay between corresponding points on the pressure-time curves as measured by the two transducers (e.g. 10%) (for example,  $Dt$  a time delay between pressure maxima may be used or alternatively, one may choose the time delay between points at which the pressure attains a fixed, arbitrarily chosen, percentage of the full range of the pressure curve). The measured pressure rises very fast and in most cases it reaches its maximum before the reflected wave has had time to overlap the forward pressure wave. It is known, that the PWV in arterial segment increases with pressure, which is an indication of gradual stiffening of the artery with pressure. By using well established viscoelastic arterial models, the analysis of the PWV for several specified percentage of full range of the pressure enables one to compute the stiffness of the vessel wall.

15

**Procedure 4: Pressure wave velocity with one pressure transducer.**

PWV measurement was determined using a single transducer :measure reflection time at two sites  $Ds$  cm apart. This reflection time was be found using one of the single pressure transducer methods described below.  $Dt$  was the difference between measured reflection times at these two points, The pressure wave PWV velocity is  $PWV = 2Ds/Dt$ .

**METHOD NO. 1: Single pressure sensor - unknown input signal**

Reference is now made to Figure 9. A single pressure sensor 4 is inserted into the blood vessel of interest 30 and positioned at point A. Pressure pulse is applied by the pulse generator 5 and data of pressure versus time  $Pa(t)$ , at point A, are obtained. The applied pressure pulse is assumed to be unknown, or the applied pressure pulse is known but the transfer function of the catheter is unknown. Subsequently, the input pressure signal entering the blood vessel is unknown.

Data analysis

The system uses the single pressure function procedure (Procedure 2) to detect the existence and location of a stenosis, aneurysm or vascular bed.

5    Output results

1. Location of stenosis, aneurysm or vascular bed.
2. Stenosis or aneurysm severity.
3. Pressure wave velocity. The velocity is calculated using Procedure 4 or assumed to be known from previous test data.

10

In-vivo experimental results

Reference is now made to Figure 10. In-vivo experiment was performed on a pig carotid using a single pressure sensor 91 inserted into the vessel via a standard 8F catheter 93. An artificial occlusion 92 was applied about 5 cm distal to the pressure sensor 91, created by

15    an external occluder balloon (Vascular Occluder, IN VIVO METRIC, CA.,U.S.A.) causing blood vessel lumen diameter reduction to about 2/3 of the original diameter (about 50% lumen area reduction) - estimation has been performed based on angiographics. An artificial flow/pressure signal has been introduced into the catheter using the syringe acted by a pistol hammer mechanism described in Figure 8. An unknown input pressure signal was applied.

20    Pressure versus time data measured by the pressure sensor 91 are shown in Figs. 25 and 26.

The two peaks shown in Figure 26 are the pressure input signal 93, and the reflected pressure signal 94. The data were processed by Procedure 2. Figure 27 shows the result of the analysis: two major peaks representing the timing and amplitude of the forward pulse

25    and the reflected pulse. The distance between the two peaks in msec (T) is measured from the graph. The velocity of the pressure wave was found - 5.5 m/sec. The distance of the stenosis from the pressure sensor is calculated using the velocity and time interval:  $0.016 \times 5.6 = 0.09$ . The distance to stenosis is therefore  $0.09/2 = 4.5$  cm, similar to the distance which was measured angiographically). The calculated reflection coefficient was  
30    found to be 0.4 . This correlates well with the calculation based on  $R_F = (A_o - A_s)/(A_o + A_s)$  presented hereinabove:  $A_o = p_{16} \text{ mm}^2$ ,  $A_s = p_{6.25}$  resulting in a reflection coefficient of

0.44.

### METHOD NO. 2: Single pressure sensor - long range stenosis

#### Data Acquisition:

- 5 The method is described in Figure 9. A single pressure sensor 4 is inserted into the blood vessel of interest 30 and positioned at point A, upstream the stenosis. The distance between the sensor and the stenosis result in a separation of the exciting pressure wave (forward wave) and the reflected wave (backward wave). Pressure pulse is applied by the pulse generator 5 and data of pressure versus time  $P_a(t)$ , at point A, are obtained.

10

#### Data analysis

- The system uses the two pressure function procedure (Procedure 1) to detect the existence and location of stenosis, aneurysm or vascular bed. No prior knowledge of the exciting signal is required. The procedure is taking advantage of the inherent separation of the forward and backward components of the signal. The procedure is modified to recognize the input signal,  $w(n)$ , from the first part of the output signal, and apply the Procedure 1 to the second part of the signal,  $s(n)$ . The system uses the method described in Figure 17 to estimate the severity of stenosis or aneurysm.
- 15

20 Input data required for using the procedure:

1. Pressure versus time function  $P_a(t)$ , measured by the single sensor 4.
2. Pressure wave velocity. The velocity was calculated using Procedure 4 or assumed to be known from previous test data.

25 Output results

1. Location of stenosis, aneurysm or vascular bed.
2. Stenosis or aneurysm severity.

#### In-vitro experimental results

- 30 Data were acquired on the in-vitro system described in Figs 5-7, with a single pressure sensor, 24a, within. Figure 28 illustrates the application of the Procedure 2 on an in-vitro

pressure data. The lower part of Figure 28 presents the pressure versus time as measured by the pressure sensor,  $Pa(t)$ , located at A. The upper part of Figure 28 presents the result of the Procedure 1, where the 2 peaks, of the input pressure wave ( $P_I$ ), and the reflected wave ( $P_R$ ) can be clearly observed. The time interval between the two peaks is calculated from Figure 28 to be 56 msec. Knowing the velocity of the pressure wave, 14 m/sec, allows calculating the stenosis location:  $0.056 \times 14 = 0.392$  m. This is a perfect match to the 40 cm distance between the transducer and the stenosis.

### METHOD NO. 3: Single pressure sensor - known input signal

10

#### Data acquisition

The method is described in Figure 9. A single pressure sensor is inserted into the blood vessel of interest 30 and positioned at point A. Pressure pulse is applied by the pulse generator 5 and data of pressure versus time  $Pa(t)$ , at point A, are obtained. The applied pressure signal is controlled and known from the pulse generator 5. The transfer function of the catheter is assumed to be known. Therefore the input pressure signal entering the blood vessel is known.

#### Data analysis

20 The system uses the dual pressure function procedure (Procedure 1) to detect the existence and location of stenosis, aneurysm or vascular bed. The system uses the method described in Figure 17 to estimate the severity of stenosis or aneurysm.

25 One could refer to the in-vitro example discussed in Method 6, and presented in Figure 20, as a demonstration of the actual method, where the upstream pressure signal is considered as a known input.

#### Input data required for using the procedure:

1. Pressure versus time function  $Pa(t)$ , measured by the sensor 4.
- 30 2. Pressure wave velocity. The velocity is assumed to be known from previous test data or calculated using Procedure 4.

3. Catheter transfer function. The pressure versus time transfer function is assumed to be known from previous test results.
4. Exciting signal (forward pressure wave). The signal magnitude, duration and shape are controlled and known by the pressure generator 5.

5

#### Output results

1. Location of stenosis, aneurysm or vascular bed.
2. Stenosis or aneurysm severity.

10

### **METHOD NO. 4: Single pressure sensor - two measuring sites**

#### Data acquisition

The method is described in Figure 19. A single pressure sensor is inserted into the blood vessel of interest and positioned at point A. Pressure pulse is applied by the pulse generator 15 5 and data of pressure versus time  $Pa(t)$ , at point A, are obtained. The pressure sensor is now moved downstream, by a known distance L and positioned at point B. The pressure generator 5 generates a similar pressure pulse, and data of pressure versus time,  $Pb(t)$ , are obtained.

20

#### Data analysis

The system uses the dual pressure function procedure (Procedure 1) described above to detect the existence and location of stenosis, aneurysm or vascular bed. The system uses the method described in Figure 17 to estimate the severity of stenosis or aneurysm. One could refer to the in-vitro example discussed in Method 6, and presented in Figure 19, as a demonstration of the actual method, where the upstream pressure signal is acquired by the same pressure sensor located in A and the downstream signal is acquired by the same pressure sensor moved to B.

25

#### Input data required for using the procedure:

- 30 1. Pressure versus time measured at location A -  $Pa(t)$ .
2. Pressure versus time measured at location B -  $Pb(t)$ .

3. Pressure wave velocity. The velocity is assumed to be known from previous test data, or evaluated using the single pressure PWV procedure.
4. Input signal (forward pressure wave). The signal magnitude, duration and shape are controlled and known by the pressure generator.

5

#### Output results

1. Location of stenosis, aneurysm or vascular bed.
2. Stenosis or aneurysm severity.

10

### METHOD NO.5: Two-pressure sensors - visual method

Reference is now made to Figure 11 and 13. Two pressure sensors 4a and 4b are inserted into the blood vessel 30 of interest via a standard connector 8 connected to a catheter 3. In another embodiment, the pressure sensors 4a and 4b may be mounted on a mutual wire or 15 catheter (e.g. Millar 2.5F dual sensor model SPC-721, Millar Instruments Inc., TX, U.S.A.). In another embodiment, the pressure sensor 4a may be a fluid filled manometer sensor connected to the catheter 3 via the connector 8. The pulse generator 5 applies a pressure pulse. Data of pressure versus time are obtained from pressure sensors 4a and 4b. Figure 10 describes a blood vessel without stenosis. Figure 13 describes a blood vessel with a 20 downstream stenosis. PWV may be either calculated using Procedure 3 or known from prior data.

#### Data analysis - in-vitro experimental results

25 Reference is now made to Figure 12 and 14. Figure 11 describes pressure changes versus time (number of samples), sampled at 5000 samples/sec. Data were obtained on the in vitro system described in Figs. 5-7. The system does not include stenosis inside the vessel, however far reflections occur from the system bath 44 right edge. Figure 12 serves as a reference data for cases where stenosis does exist in a blood vessel. The vertical axis 30 indicates the pressure values in units of mmHg. The horizontal axis indicates the number of samples. The two curves in Figure 11 indicate the pressure value at two different points

along the vessel, at the location of the two pressure sensors 24a and 24b. The dashed line is used for pressure measured by the sensor 24A and dotted line for the pressure measured by the sensor 24B.

- 5      Figure 14 describes the pressure changes versus time as explained for Figure 11. Data acquisition was preformed using the system described in Figs. 4-6, with the presence of a stenosis, as described in Figure 13. The pressure pulse is similar to the pulse generated for the case described in Figure 12 (without stenosis). When a stenosis exist in a blood vessel, a visible and detectable change in the pattern of the pressure waves can be identified. This  
10     change is caused by the reflection of the pressure wave from the occluded site. The use of two transducers allows accurate identification of the reflection point. The pressure wave created by the pressure generator 5 advances and reaches first the upstream pressure sensor 24A and later the downstream sensor 24B, so that a time delay,  $Dt$ , exist between the signal measured by the pressure sensor 24a and the signal measured by the pressure signal 24b.  
15     The pressure wave measured by the upstream sensor (24a) is ahead of the pressure measured by the downstream sensor (24b). In Figure 13, the dashed line is used for pressure measured by sensor 24A and dotted line for sensor 24B.

20     When a stenosis exist the reflected wave reaches first the downstream sensor 24B and later the upstream sensor 24A. This causes a change in the order of propagation of the two waves, so that the pressure wave measured by the downstream sensor 24b is now ahead of the other pressure wave 24a. The change in the order of the propagating waves is an indication for the existence of reflection caused by a stenosis. The point along the time axis, where the change in order of the propagating waves occurs, was used to determine the location of the stenosis.  
25

Reference is now made to Figure 15 and 16. The vertical axis represents the pressure time derivative ( $dp/dt$ ) as calculated from the data of Figure 12 and 14. The use of pressure time derivative instead of the pressure may simplify the identification of the reflection point. Figure 15 presents the pressure time derivative versus time as measured by sensors 24a and  
30     24b in the case where the system does not include stenosis. Figure 16 presents the pressure time derivative versus time obtained from the system with stenosis.

Output results

1. Location of stenosis, aneurysm or vascular bed.
2. Pressure wave velocity.

5

**METHOD NO.6: Two-pressure sensors - analytical method**

Reference is now made to Figure 11. Two pressure sensors 4a and 4b are inserted into the blood vessel 30 of interest via a standard connector 8 connected to a catheter 3. In another embodiment, the pressure sensors 4a and 4b may be mounted on a mutual wire or catheter (e.g. Millar 2.5F dual sensor model SPC-721, Millar Instruments Inc., TX, U.S.A.). In another embodiment, the pressure sensor 4a may be a fluid filled manometer sensor connected to the catheter 3 via the connector 8. The pulse generator 5 applies a pressure pulse. Data of pressure versus time are obtained from pressure sensors 4a and 4b

15

Data analysis

The system uses the dual pressure function procedure (Procedure 1) described above, to detect the existence and location of stenosis, aneurysm or vascular bed. The system uses the method described in Figure 17 to estimate the severity of stenosis or aneurysm.

20

Output results

1. Location of stenosis, aneurysm or vascular bed.
2. Stenosis or aneurysm severity.
3. Pressure wave velocity.

25

In-vitro experimental results

Figure 19 illustrates the application of the procedure on two pressure in-vitro data, where one pressure transducer was 12 cm and a second pressure transducer was located 7 cm upstream the stenosis. Figure 19a presents the pressure versus time as measured by the upstream sensor,  $Pa(t)$ , located at A, 12 cm from the stenosis. Figure 19b presents the pressure as measured by the downstream sensor,  $Pb(t)$ , located at B, 7 cm from the stenosis.

The result of the Procedure 1 is presented in Figure 19c, where the 2 peaks, of the input pressure wave (PI), and the reflected wave (PR) can be clearly observed. The time interval between the two peaks is calculated from the graph - 10 msec. Knowing the velocity of the pressure wave, 14 m/sec, allows calculating the stenosis location:  $0.01 \times 14 / 2 = 0.07$  m, which is a perfect match to the experiment setup. Stenosis severity or reflection coefficient was calculated according to the area ratio, as explained above. The calculated coefficient is 0.317. A third pressure sensor was located 2 cm from stenosis. The same procedure was applied again and results are presented in Figure 189. Calculated distance using the time difference between the peaks (3 msec) is 2.1 cm, and the reflection coefficient is 0.316. The same reflection coefficient was expected and calculated for both transducers at 2 cm and 7 cm, in reference to the same stenosis. Verification for the value of the expected reflection coefficient is offered by the equation  $R_F = (A_o - A_s) / (A_o + A_s)$  presented hereinabove:  $A_o = 16 \text{ mm}^2$ ,  $A_s = 9 \text{ mm}^2$  then  $R_F = 7/25 = 0.28$ . Moreover, applying the Procedure 2 on the same data resulted in a reflection coefficient of 0.34, and the same calculated distance, as presented in Figure 19e.

#### METHOD NO.7: Flow rate measurement

##### Data acquisition

The system used for data acquisition is described in Figure 9. A flow rate sensor (replacing the pressure transducer 4) is inserted into the blood vessel of interest 30 and positioned at point A. Pressure pulse is applied by the pulse generator 5 and data of flow rate versus time  $Q_a(t)$  at point A, are obtained.

##### Data analysis

Reference is now made to Figure 21-22, presenting data acquired on the in-vitro system described in Figs 4-7 and modified to include an ultrasonic flowmeter (model T206, Transonic Systems Inc., NY, U.S.A.) and a stenosis 55, as shown in Figure 20. Figs. 21 and 22 present the flow rate changes versus time (number of samples). A sharp increase in the flow rate when pressure excitation is applied by the pulse generator 5, followed by a gradual decay. This response is similar to the pressure signal. Therefore, all methods of

analysis described for the pressure signals are applicable. Visual inspection of Figs. 21, reveals a change in the signal development marked P2, corresponding to the reflection from a stenosis at 95 cm distance. Using the observed time delay of 683 samples (equivalent to 136.6 msec), we get  $0.1366 \times 13.9/2 = 95$  cm. Figure 25, reveals a change in the signal development marked P2, corresponding to the reflection from a stenosis at 50 cm distance. Using the observed time delay of 74.6 msec, we get  $0.0746 \times 13.9/2 = 52$  cm. These calculations are based on a pressure wave velocity, 13.9 m/sec, deduced from pressure data acquired with two pressure transducers located 5.5.cm apart, using Procedure 3, and shown in Figure 23.

10

The change in the signal, designated P2, presented in Figs. 21 and 22 is differs from the change in the pressure signals observed above. The different reflection appearance originates from the fact that a forward flow is reflected as a refraction wave, as a negative flow, therefore the superposition of the forward and backward flows result in a decrease in amplitude (' a valley') and not an increase as observed with the pressure signals.

In all the in-vitro examples given above, the PSG module was built using the presented technique of a gun pistol (Figs. 31). However, as described hereinabove, other embodiment includes the Bio-Tek , blood pressure systems calibrator Model 601A, VT, U.S.A.. Figure 28 presents data acquired on the in-vitro system described in Figs. 4-7 with two pressure transducers 24a and 24b, with a pressure excitation pulse generated by the Bio-Tek calibrator, as a step function. Figure 28 shows the step signal and the reflection from a stenosis 85 cm away. Using the derived time delay 114.2 msec , and a pressure wave velocity of 15 m/sec, the right distance is calculated. A PSG of this type is illustrated by Figure 31 in which a pump with an electromagnetic push/pull mechanism is used to control the rapid flow of fluid needed to generate a desired pressure pulse.

Alternatively, Figure 32 illustrates a PSG device having an external electromagnetic hammer giving a punch to a full-of-fluid membrane. The resulting punch causes a pressure pulse signal to be generated. Another PSG device is illustrated by Figure 33 in which two separate membrane chambers having fluid volumes. One of the chambers is high pressure

relative to the other. An external electromagnetic hammer moves or destroys a membrane separating the two chambers thereby generating the pressure signal. Finally, Figure 34 illustrates a PSG device having a two way linearly proportional flow control valve operated by a straight DC drive signals. The valve when opened releases high pressure fluid that results in the generation of a pressure signal. As can be seen from these embodiments, many different variation on flow and pressure may be utilized either alone or in combination to cause the pressure signal to be generated.

10           **METHOD NO. 8: PWV and single reflection site parameters estimation- two measuring sites.**

Data acquisition

This method is another embodiment of pressure wave velocity (PWV) and reflection site parameters (position and reflection coefficient) estimation based on two-point pressure measurement carried out inside of an artery. The pressure is measured by sensors, either simultaneously by two pressure sensors or in different time by single sensor.

In the case of the simultaneously pressure measurement two pressure sensors are placed throw fixed distance  $d$  measuring pressure versus time. Since the time measuring interval and distance between sensors are known, pressure wave velocity can be calculated. In the single sensor case the pressure is first measured in point  $a$  (upstream) and after that – in point  $b$  (downstream). The distance  $d$  between these points is known. The reflection site (in instance stenosis) is placed in point  $c$ . Time synchronization of the different measurements is performed using an external excitation short duration pulse as reference. Other methods that can also be used for synchronizing such as synchronization by a hart beat signal. After synchronization the time measuring interval and distance between the two pressure sensors are known and then PWV can be calculated

Data analysis

30       It is assume that PWV and reflection coefficient are constant. In this case:

$$\begin{aligned} S_a(t) &= S(t) + r_0 * S(t - 2 * \tau_0 - 2 * \Delta_0) \\ S_b(t) &= S(t - \tau_0) + r_0 * S(t - \tau_0 - 2 * \Delta_0) \\ \tau_0 &= d / v_0 \\ \Delta_0 &= l / v_0 \end{aligned}$$

where,

$S(t)$  - is the forward wave,

5

$S_a(t), S_b(t)$  - are pressure signals measured in point  $a$  and  $b$ , respectively;

$v_0$  - is the pressure wave velocity;

$r_0$  - is the reflection coefficient;

$d$  - is the distance between pressure sensors;

10  $l$  - is the distance between the downstream sensor and the reflection site location;

$\tau_0$  - is the from- $a$ -to- $b$  pressure wave propagation time;

$\Delta_0$  - is the from- $b$ -to- $c$  pressure wave propagation time;

Let's calculate next functions  $S_1(t, \tau), S_2(t, \tau)$ :

$$\begin{aligned} 15 \quad S_1(t, \tau) &= S_a(t) - S_b(t - \tau) = S(t) + r_0 * S(t - 2 * \tau_0 - 2 * \Delta_0) - \\ &S(t - \tau_0 - \tau) - r_0 * S(t - \tau_0 - \tau - 2 * \Delta_0) \end{aligned}$$

$$\begin{aligned} S_2(t, \tau) &= S_b(t) - S_a(t - \tau) = S(t - \tau) + r_0 * S(t - \tau_0 - 2 * \Delta_0) - \\ &S(t - \tau) - r_0 * S(t - 2 * \tau_0 - \tau - 2 * \Delta_0) \end{aligned}$$

One can see that

$$\begin{aligned} S_1(t, \tau_0) &= 1 / r_0 * S_2(t + \delta_0, \tau_0), \quad (1) \\ \delta_0 &= \tau_0 + 2 * \Delta_0. \end{aligned}$$

20

In order to estimate  $r_0, \tau_0, \Delta_0$  we define "global error function"  $E(\tau, r, \delta)$ :

$$E(\tau, r, \delta) = \int (S_1(t, \tau) - 1 / r * S_2(t + \delta, \tau))^2 dt, \quad (2)$$

and three functions  $\bar{E}(\tau), \bar{r}(\tau), \bar{\delta}(\tau)$  such that for fixed  $\tau$ :

$$\bar{E}(\tau) = E(\tau, \bar{r}(\tau), \bar{\delta}(\tau)) = \min_{r, \delta} \int (S_1(t, \tau) - 1/r * S_2(t + \delta, \tau))^2 dt,$$

where,

$\bar{r}(\tau), \bar{\delta}(\tau)$  minimize the integral (2). We'll call  $\bar{E}(\tau)$  as "partial error function".

- 5 Obviously, that following (1) the minimum of  $E(\tau, r, \delta)$  is achieved with the next parameters set ( $\tau = \tau_0; r = \min \bar{r}(\tau) = r_0; \delta = \min \bar{\delta}(\tau) = \Delta_0$ ) :

$$E(\tau_0, r_0, \Delta_0) = \bar{E}(\tau_0) = \int (S_1(t, \tau_0) - 1/r_0 * S_2(t + \Delta_0, \tau_0))^2 dt = 0 ,$$

$$\bar{E}(\tau_0) = \min_{\tau} \bar{E}(\tau) .$$

10

So, by optimal in LMS means shifting and scaling of  $S_2(t, \tau)$  relative to  $S_1(t, \tau)$  it is possible to calculate function  $\bar{E}(\tau)$ , to find its minimum and to estimate  $r_0, \tau_0, \Delta_0$ .

- 15 The simulation was carried out for "sharp" and known signal like the signals created by the exciter described in fig. 35. Two fix linked pressure sensors were used.

On fig.36 and 37 results of the numerical experiment are depicted. The excited pressure pulse  $S(t)$  was simulated without noise by the function:

$$S(t) = \beta * t^2 * e^{-\alpha t}, \alpha = 300, \beta = 15 * \alpha^2 * e^2 .$$

- 20 The signal (99) received by the down stream sensor and the signal (100) received by the upstream sensor are drawn on fig. 36.

The parameter  $\alpha$  impacts on the form of  $S(t)$  and  $\beta$  was chosen so that  $\max S(t) = 60$ .

The values of  $r_0, \tau_0, \Delta_0$  were: ,

25  $r_0 = 0.6, \tau_0 = 2ms, \Delta_0 = 3ms,$

PWV was  $v_0 = 15m/s$  and, consequently,

$$d = 3\text{cm}, l = 4.5\text{cm},$$

respectively, the sampling frequency was  $f=5000 \text{ Hz}$ .

5

The  $v_0, r_0, l$  were evaluated by the proposed algorithm and the accurate values were received:

$$v_0 = 15\text{m/s}, r_0 = 0.6004, l = 4.5\text{cm}.$$

Fig. 37 describes the function  $\bar{E}(\tau)$ . The minimum of  $\bar{E}(\tau)$  is achieved by  $\tau = \tau_0 = 2\text{ms}$ .

10

Reference is now made to Figs. 38, 39. The same pressure signal  $S(t)$  with ~5% additive Gaussian white noise and the partial error function  $\bar{E}(\tau)$  are depicted. Fig. 38 shows the signals received by the two pressure sensors. Fig 39 shows the error function  $E(t)$ . 10 trials were made to evaluate average values and standard deviation:

15

$$\tilde{v}_0 = 15.33 \pm 1.5\text{m/s}, \tilde{r}_0 = 0.78 \pm 0.05, \tilde{l} = 4.55 \pm 1.33\text{cm}.$$

Same assessment was carried out using low pass FIR filter with passband  $0 - 200\text{Hz}$  :

20

$$\tilde{v}_0 = 15.06 \pm 1.01\text{m/s}, \tilde{r}_0 = 0.63 \pm 0.03, \tilde{l} = 4.37 \pm 0.41\text{cm}.$$

The parameters estimation errors are:

$$\epsilon_{v_0} = 0.4\%, \epsilon_{r_0} = 5\%, \epsilon_l = 3\%, \text{ respectively.}$$

25

### IN VITRO EXPERIMENTS

The algorithm performance was tested by in-vitro experiments using the in vitro test apparatus described in fig. 5 . Different type of stenosis and distance  $l$  were exploited for testing purpose. The distance between the pressure sensors was varied as well.

30

Experiment 1 (with catheter of 10 cm length)

Two types of stenosis were used:

- full stenosis, 100%;
- stenosis 1 mm inner diameter, 85% stenosis, .

5

The sensors were fixed through either 3 cm or 1 cm. The fluid is a mixture of 40% glycerin and 60% water. No flow. The exciter described in fig. 35 was used.

Reference is now made to figs. 40 and 41 illustrating an example of the results of the  
10 in-vitro data processing. Fig. 40 describes the reflected signals, Fig. 41 describes the minimal error function. The impact pressure pulse  $S(t)$  was filtered by 0-200 HZ passband low pass FIR filter. The scenario was defined by the next set parameters:

$$v_0 \approx 14 \text{ m/s}, r \approx 1 (\text{full stenosis}), d = 3 \text{ cm}, l = 4 \text{ cm}, f = 5000 \text{ Hz}.$$

15

It's significant to emphasize the proposed algorithm is of the discrete-time-type. So the error of time-delay measurements is no less than  $\Delta t = 1/(2 * f) = 0.1 \text{ ms}$ . In the case of the close placed sensors,  $d = 1 \text{ cm}$ , it yields about 14% time-delay estimation error. The results of in-vitro data processing are summarized in Table 1.

20

Table 1

Stenosis/ $d_0$	Algorithm results			$l \text{ cm}$	No. of experiments
	$\tilde{v}_0 \text{ m/s}$	$\tilde{r}_0$	$\tilde{l} \text{ cm}$		
Full 3cm	13.64	0.78	3.74	4	4
	$\pm$	$\pm$	$\pm$		
	0	0.08	0.05		
Full 1cm	11.88	0.75	3.3	4	4
	$\pm$	$\pm$	$\pm$		
	1.25	0.06	0.46		

Full 1cm	11.25 $\pm$ 1.44	0.82 $\pm$ 0.07	2.4 $\pm$ 0.4	3	4
1mm 3cm	13.26 $\pm$ 0.66	0.38 $\pm$ 0.03	3.9 $\pm$ 0.21	4	3
1mm 1cm	12.5 $\pm$ 0	0.57 $\pm$ 0.08	2.81 $\pm$ 0.09	4	3

The accuracy of the velocity estimation is worse for  $d=1$  cm case on account of time-discretization problem mentioned above. The stenosis position error is about 5% for  $d=3$  cm and about 25% for  $d=1$  cm case. The calculated values of the reflection coefficient are consistently only for  $d=3$  cm. In general, the in-vitro data processing results seem encouraging.

#### Experiment 2 (With catheter of 1 m length)

10 The algorithm performance was tested by in-vitro experiments. Different type of stenosis and distance  $l$  were exploited for testing purpose. The distance between the pressure sensors was 3 cm.. The impact pressure pulse  $S(t)$  was filtered by 0 – 200 Hz passband low pass FIR filter. The scenario was defined by the next set parameters:  
 $v_0 \approx 14 \text{ m/s}$ ,  $r \approx 1$  (full \_ stenosis),  $d = 3 \text{ cm}$ ,  $l = 4 \text{ cm}$ ,  $f = 5000 \text{ Hz}$ .

15 Two types of stenosis were used: full stenosis , 100%; and 1mm inner diameter, 85% stenosis.

The sensors were fixed at the distance 3 cm apart. It's significant to emphasize the proposed algorithm is of the discrete-time-type.

20 Reference is now made to figs 42, 43,44,45 illustrating the test data processing when an excited signal is generated together with pressure wave signals simulating the heart beats.

Signal configuration which illustrate the reflections induced by the full stenosis are shown in the Fig.42. The pressure wave caused by the pump simulating the heart beats with peaks induced by exciter are shown in the Fig. 43. The peaks can hardly be observed. Fig. 44 show the excitation signal combined with the pressure wave signal enlarged from Fig. 43. The estimated Error-function E(t) is illustrated in Fig. 45. The results of in-vitro data processing are summarized in Table 2.

Stenosis/ $d_0$	$\tilde{V}_0$ m/s	Processing results			No. of trials
		$\tilde{r}_0$	$\tilde{l}$ cm	$l$ cm	
Full stenosis 3cm	14.66	0.67	5.34		
	$\pm$	$\pm$	$\pm$	4	3
	0.69	0.05	1.47		
Full 3cm	14.01	0.64	4.37		
	$\pm$	$\pm$	$\pm$	4	3
	1.8	0.03	0.6		

#### Experiment 3 (with catheter of 120 mm length)

The set up of the experiments is similar to that of experiment 2 except that the catheter length 10 is 120 mm. The experiments includes different types of stenosis . In some of the experiments there was no flow. In others there was a flow generated by a pump to simulate heart beats. The results of the experiments are represented in tables 3 -7.

Table 3

Stenosis status	$\tilde{v}_0$ m/s	$\tilde{r}_0$	$\tilde{l}$ cm	$l$ cm	Trials numbers
50% blunt	14.3182 $\pm 0.71868$	0.56652 $\pm 0.026203$	3.715 $\pm 0.23787$	4	10
	15.1515 $\pm 0.50253$	0.57887 $\pm 0.039535$	1.8308 $\pm 0.12166$	2	11
	16.1905 $\pm 0.81327$	0.56918 $\pm 0.016368$	1.1407 $\pm 0.1212$	1	7

5 Table 4

Stenosis status	$\tilde{v}_0$ m/s	$\tilde{r}_0$	$\tilde{l}$ cm	$l$ cm	Trials
50% conic	14.0083 $\pm 0.63694$	0.52218 $\pm 0.015009$	3.4278 $\pm 0.1915$	4	11
	15.0337 $\pm 0.76052$	0.57887 $\pm 0.039535$	1.8308 $\pm 0.12166$	2	9
	15.2778 $\pm 0.64876$	0.54371 $\pm 0.021772$	1.1865 $\pm 0.12077$	1	12

Table 5

Stenosis status	$\tilde{v}_0$ m/s	$\tilde{r}_0$	$\tilde{l}$ cm	$l$ cm	Trials
50% conic with pump	14.5455 ±0.78727	0.51385 ±0.017599	3.5118 ±0.23068	4	3
	15.2381 ±0.62995	0.54284 ±0.017675	1.1755 ±0.11623	1	6

Table 6

Stenosis status	$\tilde{v}_0$ m/s	$\tilde{r}_0$	$\tilde{l}$ cm	$l$ cm	Trials
50% blunt with pump	14.3182 ± 0.72887	0.54818 ± 0.020949	3.707 ± 0.2397	4	8
	15.2083 ±0.58927	0.56864 ±0.03887	1.8179 ±0.14975	2	8
	15.3333 ±0.74537	0.59329 ±0.016772	1.064 ±0.13654	1	5

Table 7

Stenosis and probe's properties	$\tilde{l}_0$	$\tilde{r}_0$	$l_0$	Trials number
Stenosis ID=2 mm distance between the sensors 1 cm with flow	2.1029+-0.2873	0.66066+-0.01634	2	10
Stenosis ID=1 mm distance between the sensors 1 cm. with flow	1.8469+-0.00625	0.62828+-0.022174	2	5
Stenosis ID=2 mm distance between the sensors 3 cm with flow	2.0485+-0.3105	0.52237+-0.02768	2	11
Stenosis ID=2 mm distance between the sensors 3 cm with flow	2.1023+-0.0056	0.57051+-0.01792	2	6

It will be understood that certain features and sub-combinations are of utility and may be employed without reference to other features and sub-combinations as they are outlined within the claims. While the preferred embodiment and application of the invention has been described, it is apparent to those skilled in the art that the objects and features of the present invention are only limited as set forth in claims attached hereto.

WHAT IS CLAIMED IS:

1. An apparatus for detecting, locating and characterizing changes in a tubular conduit system within a living body for transferring fluids, said apparatus comprising:
  - 5 a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said tubular conduit system;
  - a signal sensor operative to receive said probe signal following transmission into said tubular conduit system;
  - 10 a processor unit operatively connected to said signal sensor;
  - a program for controlling the processor unit;
  - said processor unit operative with said program to receive said probe signal following transmission through said tubular conduit system:
  - 15 identify changes in said probe signal;
  - detect characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal; and
  - 20 recognize and assign a label said characteristic of said tubular conduit said system.
2. The apparatus according to claim 1, wherein said processor unit is operative to select a method from a plurality of methods to identify changes in said probe signal and therefrom detect changes in said tubular conduit system.
3. The apparatus according to claim 1, wherein said tubular conduit system is a blood vessel system and said processor unit is operative to detect changes in arterial characteristics.
4. The apparatus according to claim 3 wherein said processor unit is operative to detect aneurysms.
- 30 5. The apparatus according to claim 3 wherein said processor unit is operative to detect stenosis.

6. The apparatus according to claim 3 wherein said processor unit is operative to detect arterial occlusions.

5 7. The apparatus according to claim 1 wherein said signal generator is a pressure signal generator.

8. The apparatus according to claim 1 wherein said signal generator is a flow signal generator.

10 9. The apparatus according to claim 7 wherein said signal sensor is a pressure sensor.

15 10. The apparatus according to claim 8 wherein said signal sensor is a pressure sensor.

11. The apparatus according to claim 3 wherein said signal generator is a pressure signal generator;

12 said signal sensor is a pressure signal sensor; and

20 said processor unit is operative to receive a heart beat signal; and synchronize receipt of said probe signal with said heart beat signal.

12. The apparatus according to claim 3 wherein said probe signal is a plurality of discrete signals;

25 said processor unit is operative to sample said discrete signals and receive pressure wave velocity data.

13. The apparatus according to claim 12 wherein said processor unit is operative to perform a single pressure function using said discrete signals and said pressure wave 30 velocity data.

14. The apparatus of claim 13 wherein said processor unit when performing said single pressure function is operative to calculate an allpass value and a cepstrum value from said minimum phase component;

5 separate a regular part and a singular part of said cepstrum value, where said singular part and said regular part form said pressure wave;

calculate an exponential function of singular part;

evaluate a second peak time delay with respect to a forward found in said pressure signal;

10 evaluate a coefficient by calculation of a second peak amplitude to determine an arterial characteristic;

evaluate a location of said arterial characteristic.

15. The apparatus of claim 3 wherein said signal sensor includes two sensing transducers disposed in spaced apart relation.

16. The apparatus of claim 15 wherein said processor unit is operative to receive a forward pressure wave signal from a first transducer and a probe signal represented by a plurality of discrete signals sampled overtime.

20 17. The apparatus according to claim 16 wherein said processor unit is operative to perform a dual pressure function.

18. The apparatus of claim 17 wherein said processor unit when performing said dual pressure function is operative to:

25 calculate an allpass component and cepstrum component of a minimum phase component of said forward pressure wave signal received from said signal sensor;

apply an inverse filtering of said forward pressure wave signal;

apply smoothing by a B-spline function;

detect a forward peak location by a global maximum calculation;

30 receive a threshold value;

detect a second peak location by comparison with said threshold, where said

threshold is derived from a forward peak maximum value and minimum size of a characteristic;

evaluate a second peak time delay with respect to said forward peak;

evaluate a reflection coefficient by calculating a forward and reflected peak area;

5 and

evaluate a location of said characteristic.

19. The apparatus according to claim 15 wherein said processor unit is operative to calculate a pressure wave velocity from a pressure wave sensed by said first and second transducers.

20. The apparatus according to claim 3 wherein said signal sensor is movable between at least two positions relative to said tubular conduit system and said processor unit is operative to calculate a pressure wave velocity from signals received from said two positions.

21. The apparatus according to claim 1 wherein said processor unit includes an analog to digital convertor.

20 22. The apparatus according to claim 1 wherein said signal sensor includes a signal conditioner.

23. The apparatus according to claim 1, wherein said tubular conduit system is a urinary vessel system and said processor unit is operative to detect changes in urinary tract characteristics.

24. The apparatus according to claim 1, wherein said processor unit is further operative to ascertain and assign a value corresponding to the location and size of said characteristic of said tubular conduit.

30

25. A processor apparatus for detecting, locating and characterizing changes in a

tubular conduit system within a living body for transferring fluids for use with a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said tubular conduit system and a signal sensor operative to receive said probe signal following transmission into said tubular conduit system, said processor apparatus comprising:

- 5            a processor unit operatively connected to said signal sensor;
- a program for controlling the processor unit;
- said processor unit operative with said program to receive said probe signal following transmission through said tubular conduit system:
- 10            identify changes in said probe signal;
- detect characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal;
- recognize and assign a label said characteristic of said tubular conduit said system; and
- 15            ascertain and assign a value corresponding to the location and size of said characteristic of said tubular conduit.

26.          The apparatus according to claim 25, wherein said processor unit is operative to select a method from a plurality of methods to identify changes in said probe signal and  
20            therefrom detect changes in said tubular conduit system.

27.          The apparatus according to claim 25, wherein said tubular conduit system is a blood vessel system and said processor unit is operative to detect changes in arterial characteristics.

25            28.          The apparatus according to claim 27 wherein said processor unit is operative to detect aneurysms.

29.          The apparatus according to claim 27 wherein said processor unit is operative to  
30            detect stenosis.

30. The apparatus according to claim 27 wherein said processor unit is operative to detect arterial occlusions.

31. The apparatus according to claim 27 wherein said signal generator is a pressure signal generator, and said signal sensor is a pressure signal sensor; said processor unit is operative to receive a heart beat signal; and synchronize receipt of said probe signal with said heart beat signal.

32. The apparatus according to claim 27 wherein said probe signal is a plurality of discrete signals; said processor unit is operative to sample said discrete signals and receive pressure wave velocity data.

33. The apparatus according to claim 32 wherein said processor unit is operative to perform a single pressure function using said discrete signals and said pressure wave velocity data.

34. The apparatus of claim 33 wherein said processor unit when performing said single pressure function is operative to calculate an allpass value and a cepstrum value from said minimum phase component.

35. The apparatus of claim 33 wherein said processor unit when performing said single pressure function is further operative to separate a regular part and a singular part of said cepstrum value, where said singular part and said regular part form said pressure wave.

36. The apparatus of claim 33 wherein said processor unit when performing said single pressure function is further operative to calculate an exponential function of singular part.

37. The apparatus of claim 33 wherein said processor unit when performing said single pressure function is further operative to evaluate a second peak time delay with respect to a forward found in said pressure signal.

38. The apparatus of claim 33 wherein said processor unit when performing said single pressure function is further operative to evaluate a coefficient by calculation of a second peak amplitude to determine an arterial characteristic.

5 39. The apparatus of claim 27 wherein said processor unit when performing said single pressure function is further operative to evaluate a location of said arterial characteristic.

10 40. The apparatus of claim 27 wherein said signal sensor includes two sensing transducers disposed in spaced apart relation and said processor unit is operative to receive a forward pressure wave signal from a first transducer and a probe signal represented by a plurality of discrete signals sampled overtime.

15 41. The apparatus according to claim 40 wherein said processor unit is operative to calculate a pressure wave velocity from a pressure wave sensed by said first and second transducers.

42. The apparatus according to claim 40 wherein said processor unit is operative to perform a dual pressure function.

20 43. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is operative to calculate an allpass component and cepstrum component of a minimum phase component of said forward pressure wave signal received from said signal sensor.

25 44. The apparatus of claim 42 wherein said processor unit when performing said dual pressure function is further operative to apply an inverse filtering of said forward pressure wave signal.

30 45. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is further operative to apply smoothing by a B-spline function.

46. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is further operative to detect a forward peak location by a global maximum calculation.

5

47. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is further operative to receive a threshold value.

48. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is further operative to detect a second peak location by comparison with said threshold, where said threshold is derived from a forward peak maximum value and minimum size of a characteristic.

49. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is further operative to evaluate a second peak time delay with respect to said forward peak;

50. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is further operative to evaluate a reflection coefficient by calculating a forward and reflected peak area.

51. The apparatus of claim 41 wherein said processor unit when performing said dual pressure function is further operative to evaluate a location of said characteristic.

25 52. The apparatus according to claim 41 wherein said processor unit is operative to calculate a pressure wave velocity from a pressure wave sensed by said first and second transducers.

30 53. The apparatus according to claim 27 wherein said signal sensor is movable between at least two positions relative to said tubular conduit system and said processor unit is operative to calculate a pressure wave velocity from signals received from said two

positions.

54. A method for using a computer to detect, locate and characterize changes in a tubular conduit system within a living body for transferring fluids wherein said computer is operatively connected to a signal generator configured to transmit into said tubular conduit a probe signal that changes in response to encountering changes in said tubular conduit system and a signal sensor operative to receive said probe signal following transmission into said tubular conduit system, said method comprising the steps of:

10 receiving said probe signal following transmission through said tubular conduit system;

identify changes in said probe signal;

detecting characteristics of said tubular conduit system, said characteristics of said tubular conduit system being derived from changes in said probe signal; and

15 recognizing and assigning a label said characteristic of said tubular conduit said system.

55. The method according to claim 53 including the steps of ascertaining and assigning a value corresponding to the location and size of said characteristic of said tubular conduit.

20

56. The method according to claim 53 further including selecting a process from a plurality of processes identifying changes in said probe signal and therefrom detecting changes in said tubular conduit system.

25

57. The method according to claim 53, wherein said tubular conduit system is a blood vessel system, said method further including detecting changes in arterial characteristics.

58. The method according to claim 56 including detecting aneurysms.

30

59. The method according to claim 56 including detecting stenosis.

60. The method according to claim 56 including detecting arterial occlusions.
61. The method according to claim 56 wherein said signal generator is a pressure signal generator, and said signal sensor is a pressure signal sensor; said method including receiving a heart beat signal; and synchronizing receipt of said probe signal with said heart beat signal.  
5
62. The method according to claim 56 wherein said probe signal is a plurality of discrete signals; said method including sampling said discrete signals and receiving pressure wave velocity data.  
10
63. The method according to claim 61 including the steps of performing a single pressure function using said discrete signals and said pressure wave velocity data.
- 15 64. The method of claim 62 wherein said performing step includes the step of calculating an allpass value and a cepstrum value from said minimum phase component.
65. The method of claim 62 wherein said performing step includes the step of separating a regular part and a singular part of said cepstrum value, where said singular part and said regular part form said pressure wave.  
20
66. The method of claim 62 wherein said performing step includes the step of calculating an exponential function of singular part.
- 25 67. The method of claim 62 wherein said performing step includes the step of evaluating a second peak time delay with respect to a forward found in said pressure signal.
68. The method of claim 62 wherein said performing step includes the step of evaluating a coefficient by calculation of a second peak amplitude to determine an arterial characteristic.  
30

69. The method of claim 62 wherein said performing step includes the step of evaluating a location of said arterial characteristic.
- 5 70. The method of claim 57 wherein said signal sensor includes two sensing transducers disposed in spaced apart relation, said method includes the step of receiving a forward pressure wave signal from a first transducer and a probe signal represented by a plurality of discrete signals sampled overtime.
- 10 71. The method according to claim 69 further including the step of calculating a pressure wave velocity from a pressure wave sensed by said first and second transducers.
72. The method according to claim 70 further including the step of performing a dual pressure function.
- 15 73. The method of claim 71 wherein said performing step includes the step of calculating an allpass component and cepstrum component of a minimum phase component of said forward pressure wave signal received from said signal sensor.
- 20 74. The method of claim 71 wherein said performing step includes the step of applying an inverse filtering of said forward pressure wave signal.
75. The method of claim 72 wherein said performing step includes the step of applying smoothing by a B-spline function.
- 25 76. The method of claim 72 wherein said performing step includes the step of detecting a forward peak location by a global maximum calculation.
77. The method of claim 72 wherein said performing step includes the step of receiving a threshold value.
- 30 78. The method of claim 72 wherein said performing step includes the step of

detecting a second peak location by comparison with said threshold, where said threshold is derived from a forward peak maximum value and minimum size of a characteristic.

79. The method of claim 72 wherein said performing step includes the step of  
5 evaluating a second peak time delay with respect to said forward peak;

80. The method of claim 72 wherein said performing step includes the step of  
evaluating a reflection coefficient by calculating a forward and reflected peak area.

10 81. The method of claim 72 wherein said performing step includes the step of  
evaluating a location of said characteristic.

15 82. The method of claim 72 wherein said performing step includes the step of  
calculating a pressure wave velocity from a pressure wave sensed by said first and second  
transducers.

83. The method according to claim 55 wherein said signal sensor is movable between  
at least two positions relative to said tubular conduit system, said method including the step  
of calculating a pressure wave velocity from signals received from said two positions.

20 84. The method of claim 58, comprising determining the geometrical shape of the  
stenosis.

25 85. The method of claim 83 comprising the steps of comparing the pressure signal  
proximal to the stenosis to the pressure signal distal to the stenosis so as determine the  
geometrical shape of the stenosis.

86. The method of claim 83, comprising the steps of determining the reflection of  
the stenosis.

30

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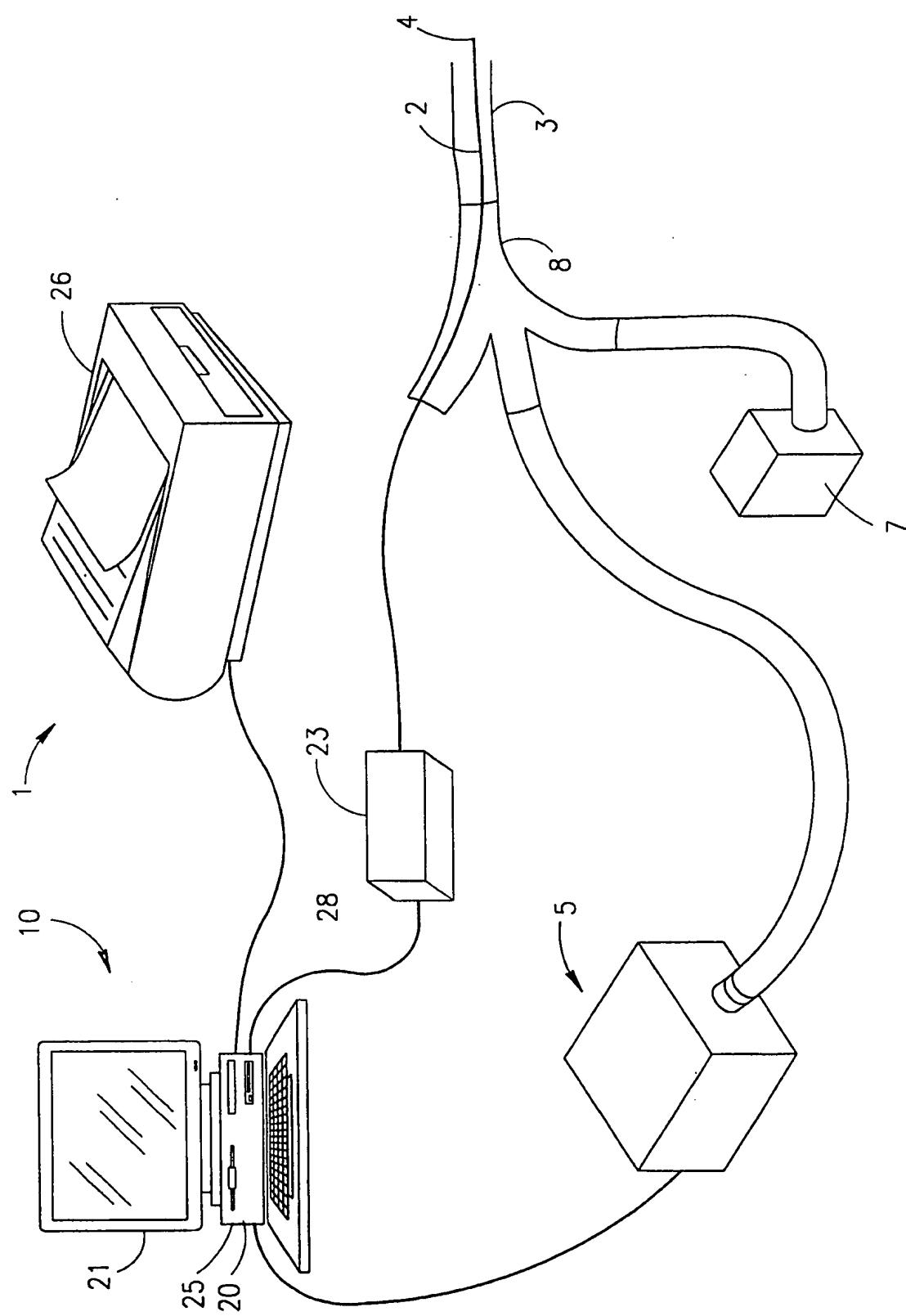


FIG.1

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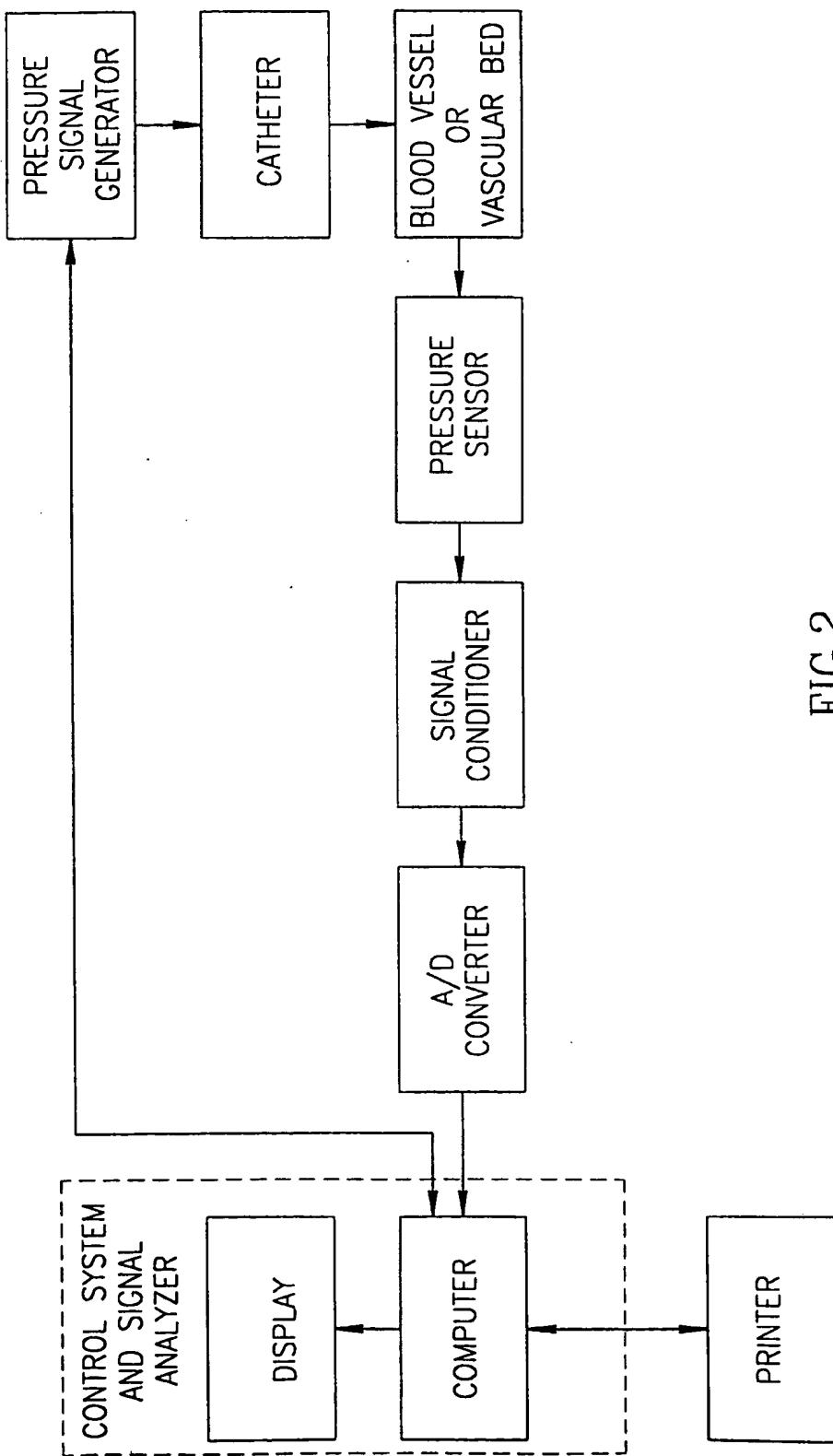
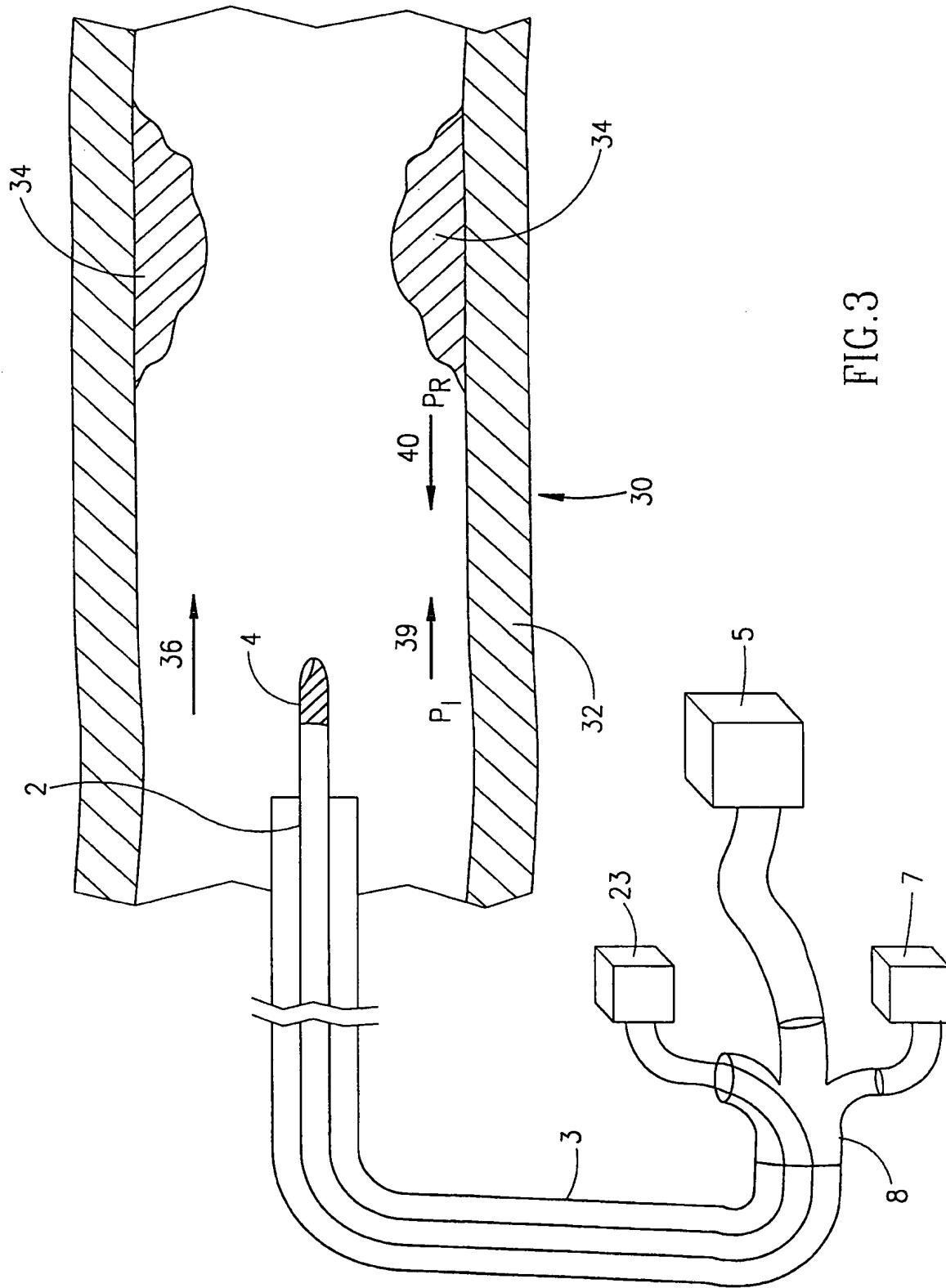


FIG.2

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SUBSTITUTE SHEET (RULE 26)

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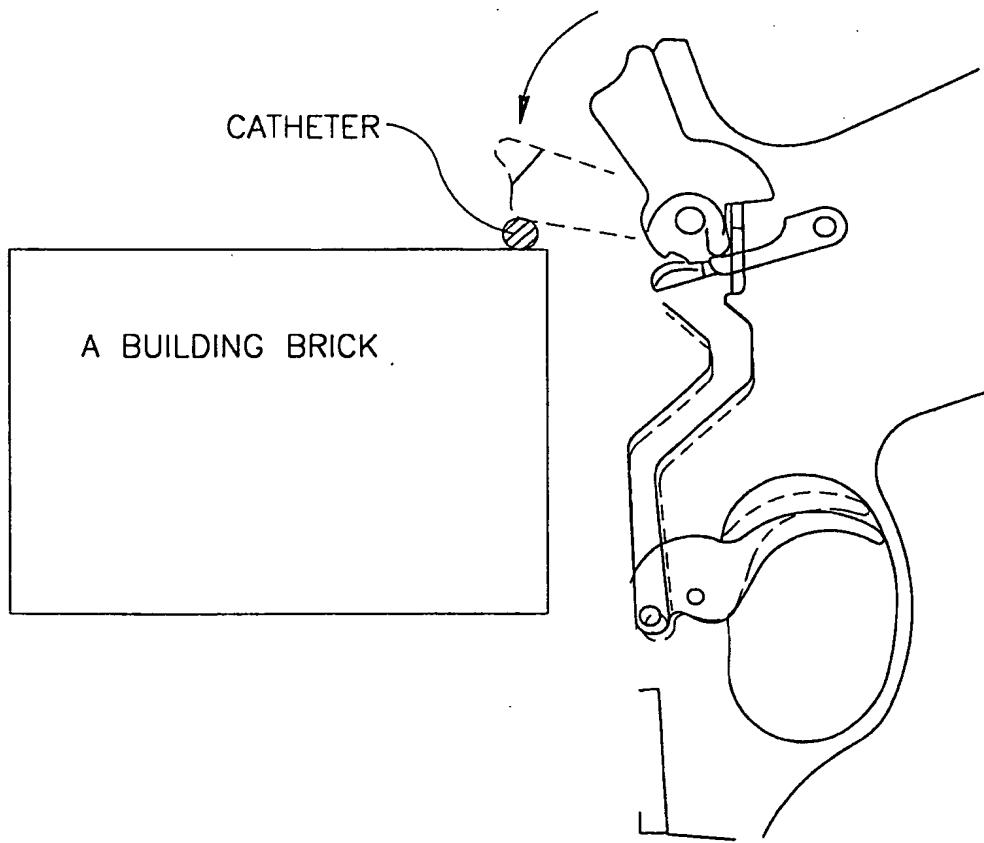


FIG.4

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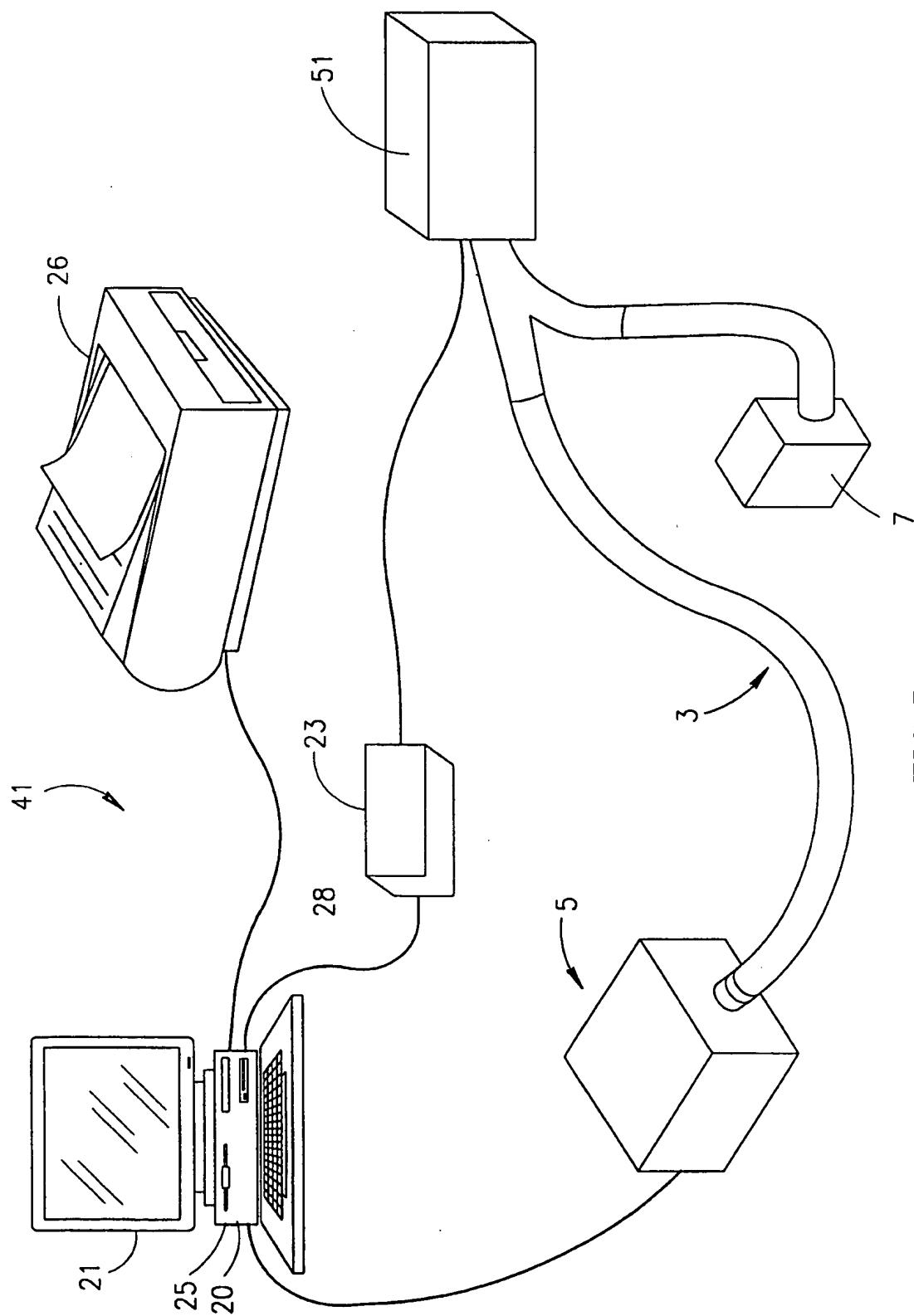


FIG.5

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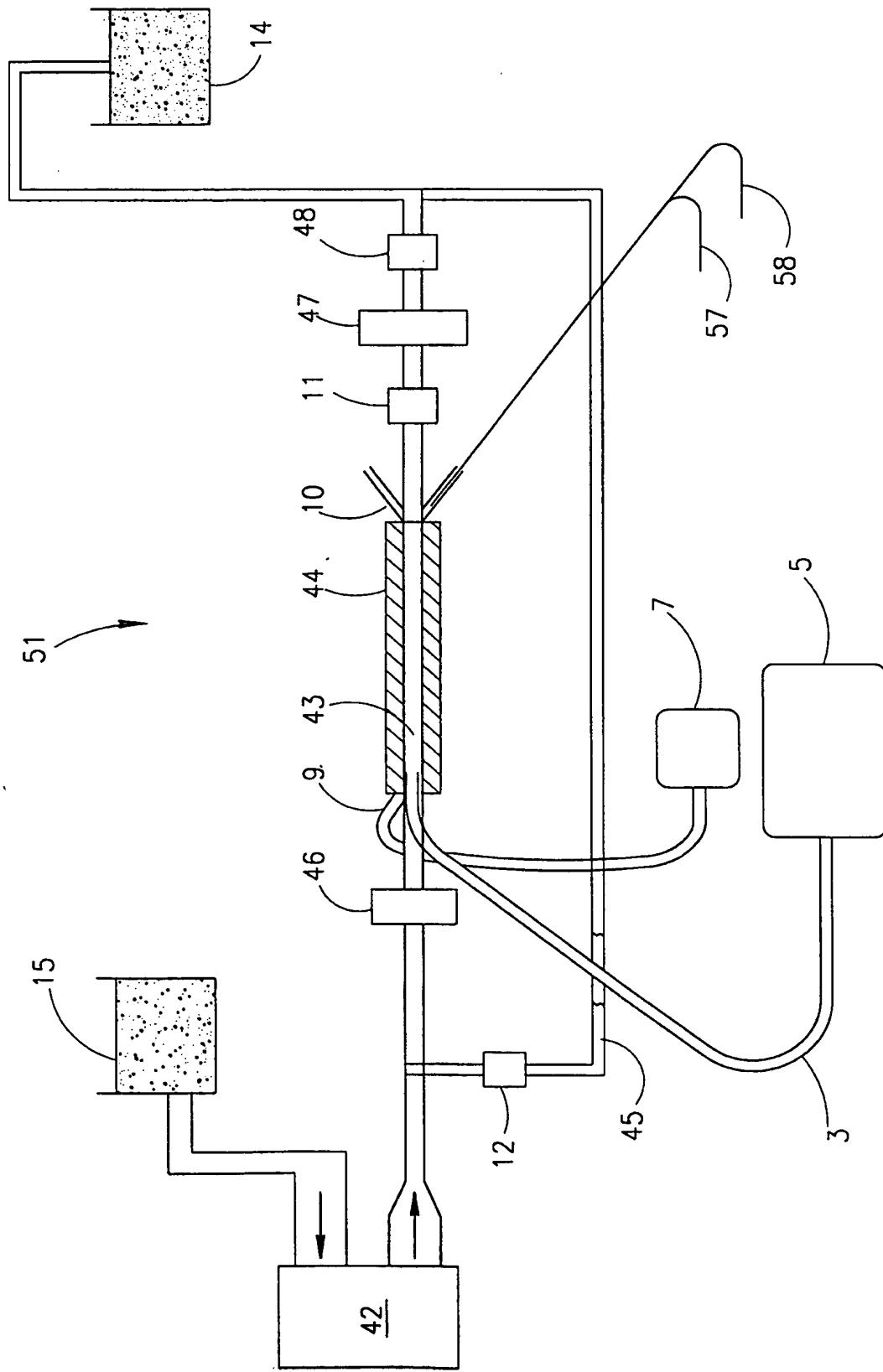


FIG. 6

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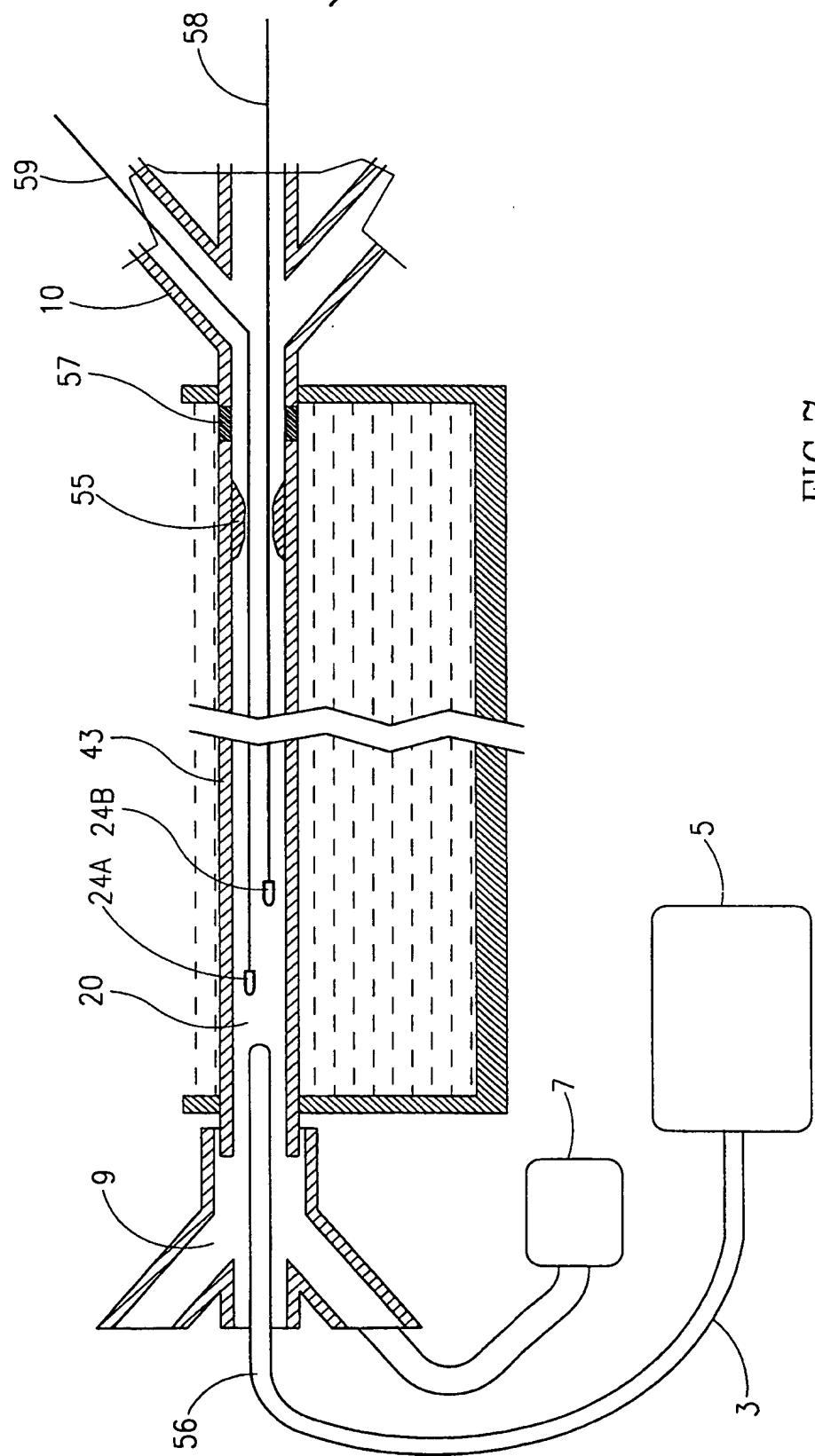


FIG. 7

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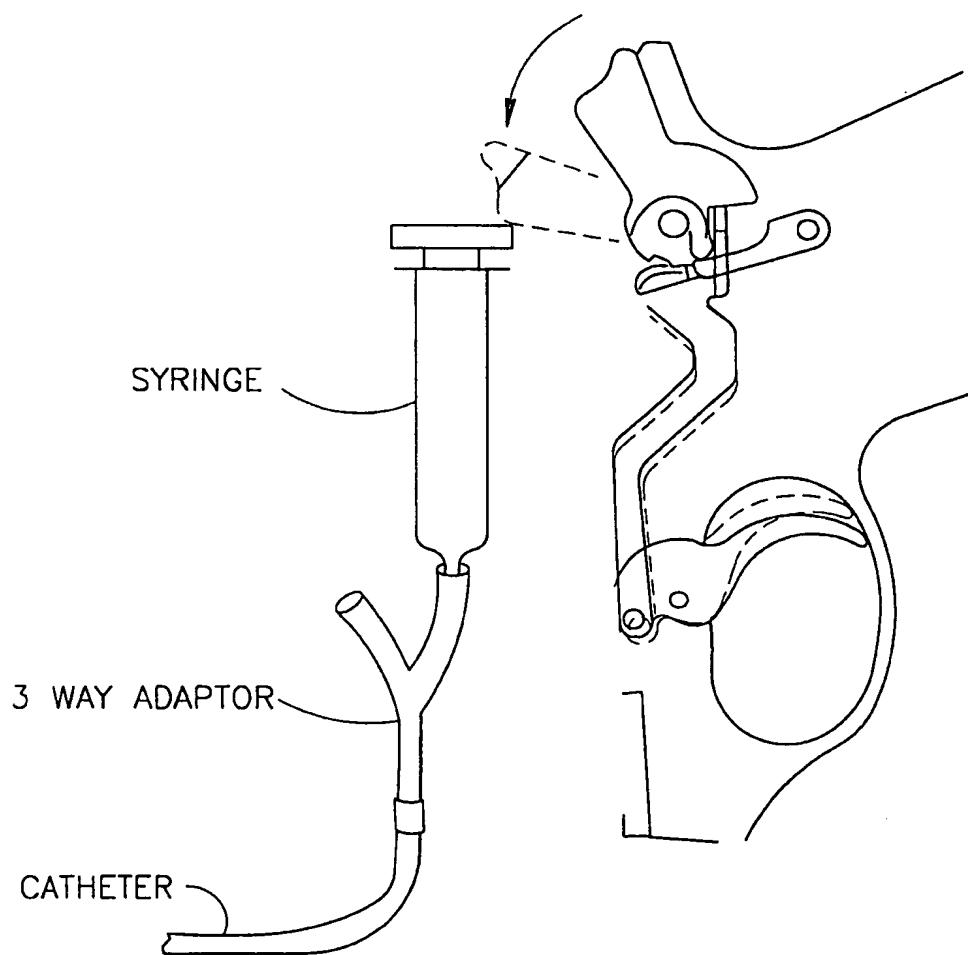


FIG.8

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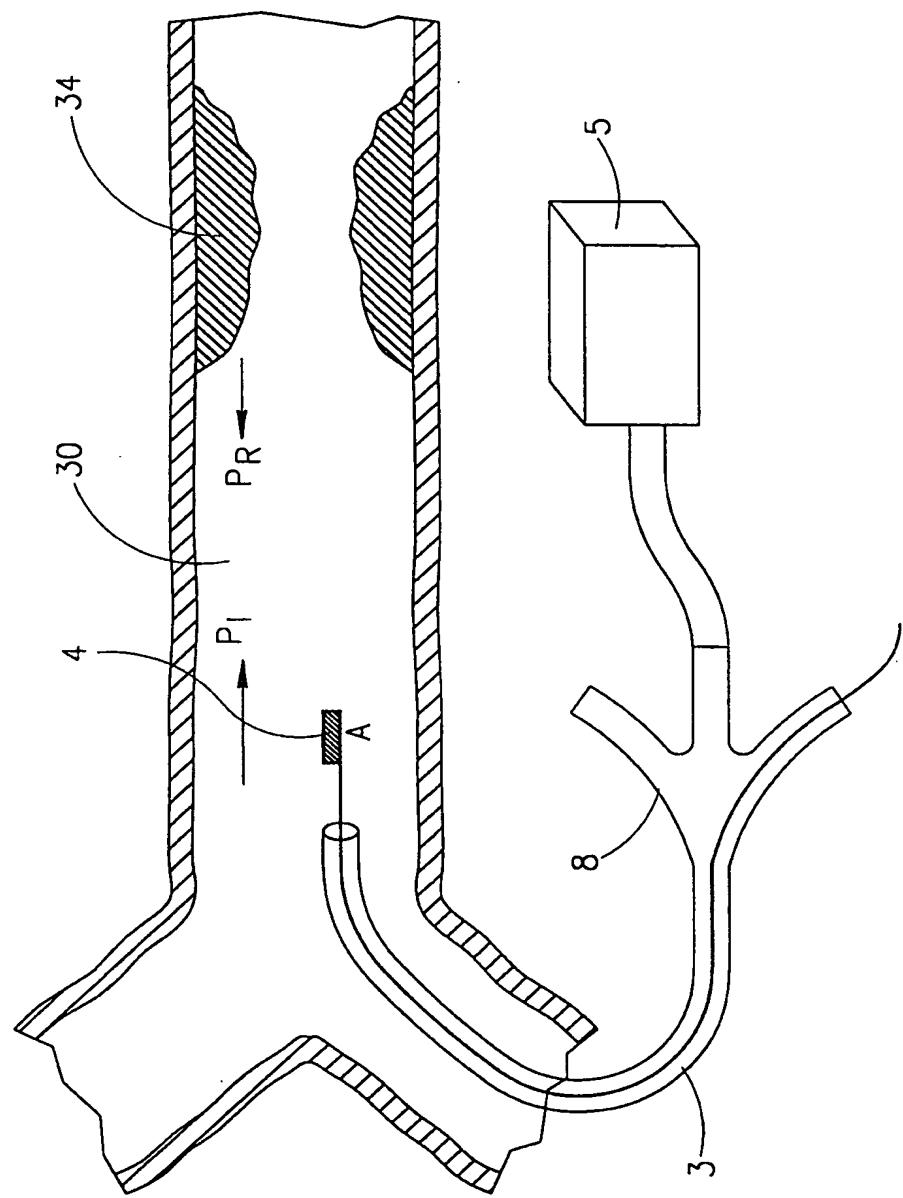


FIG. 9

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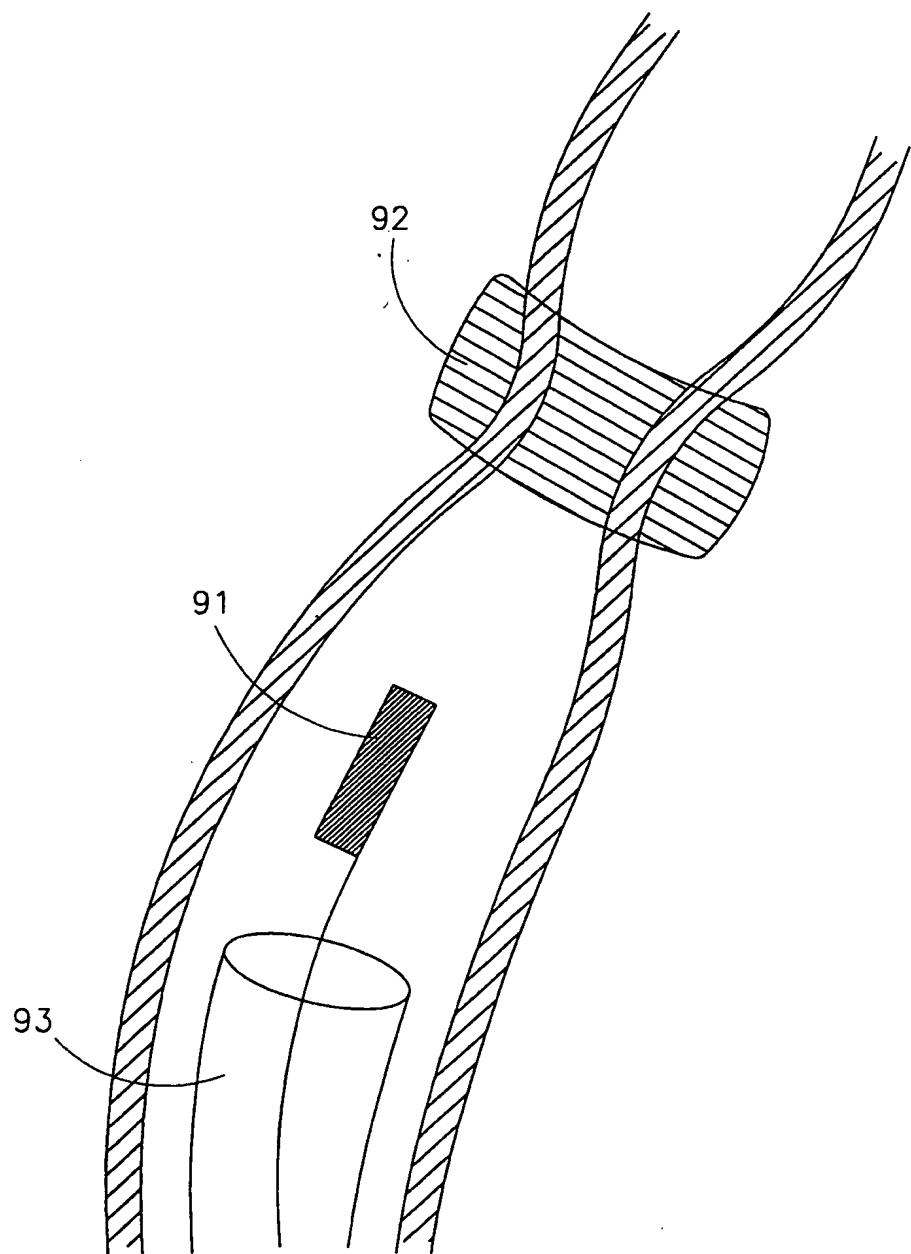


FIG.10

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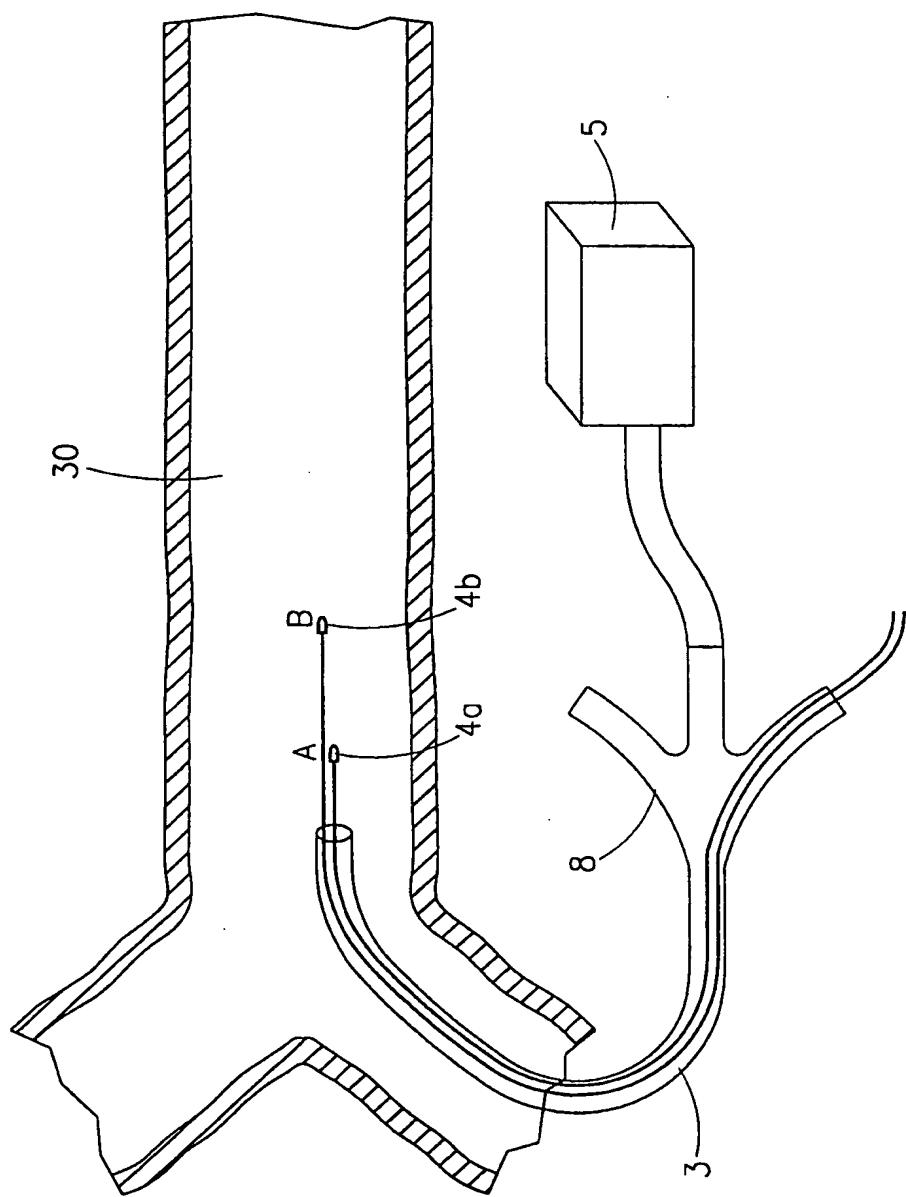


FIG.11

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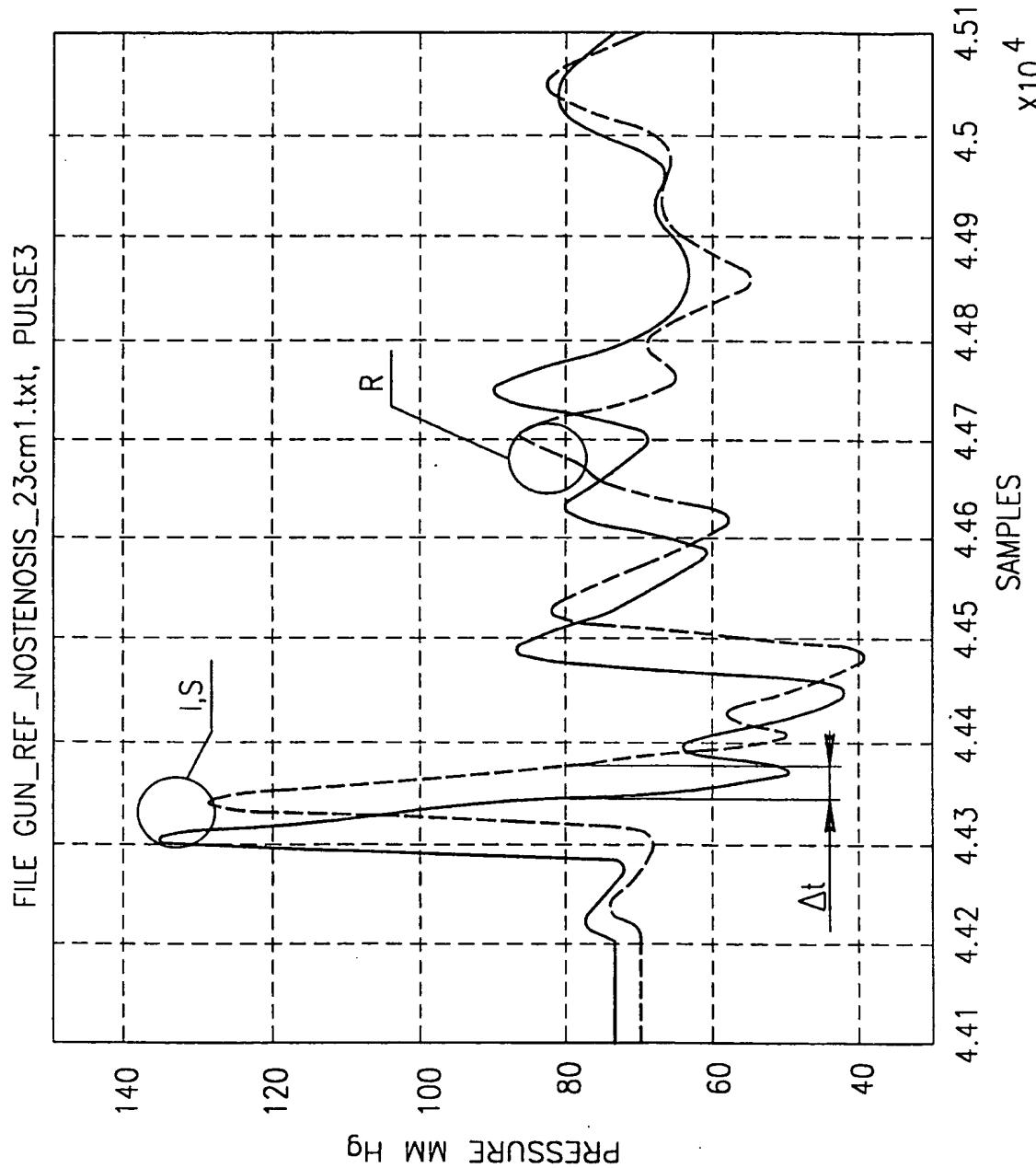


FIG.12

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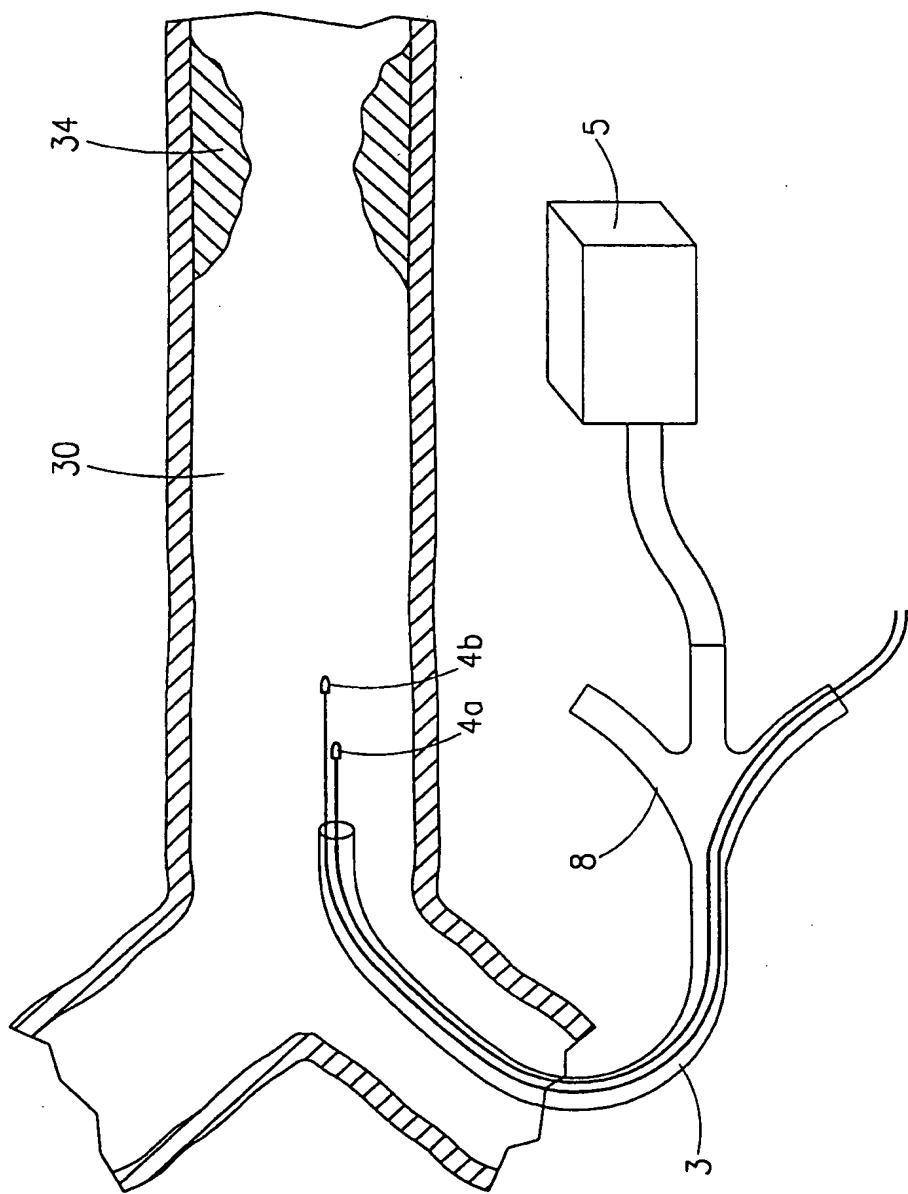


FIG. 13

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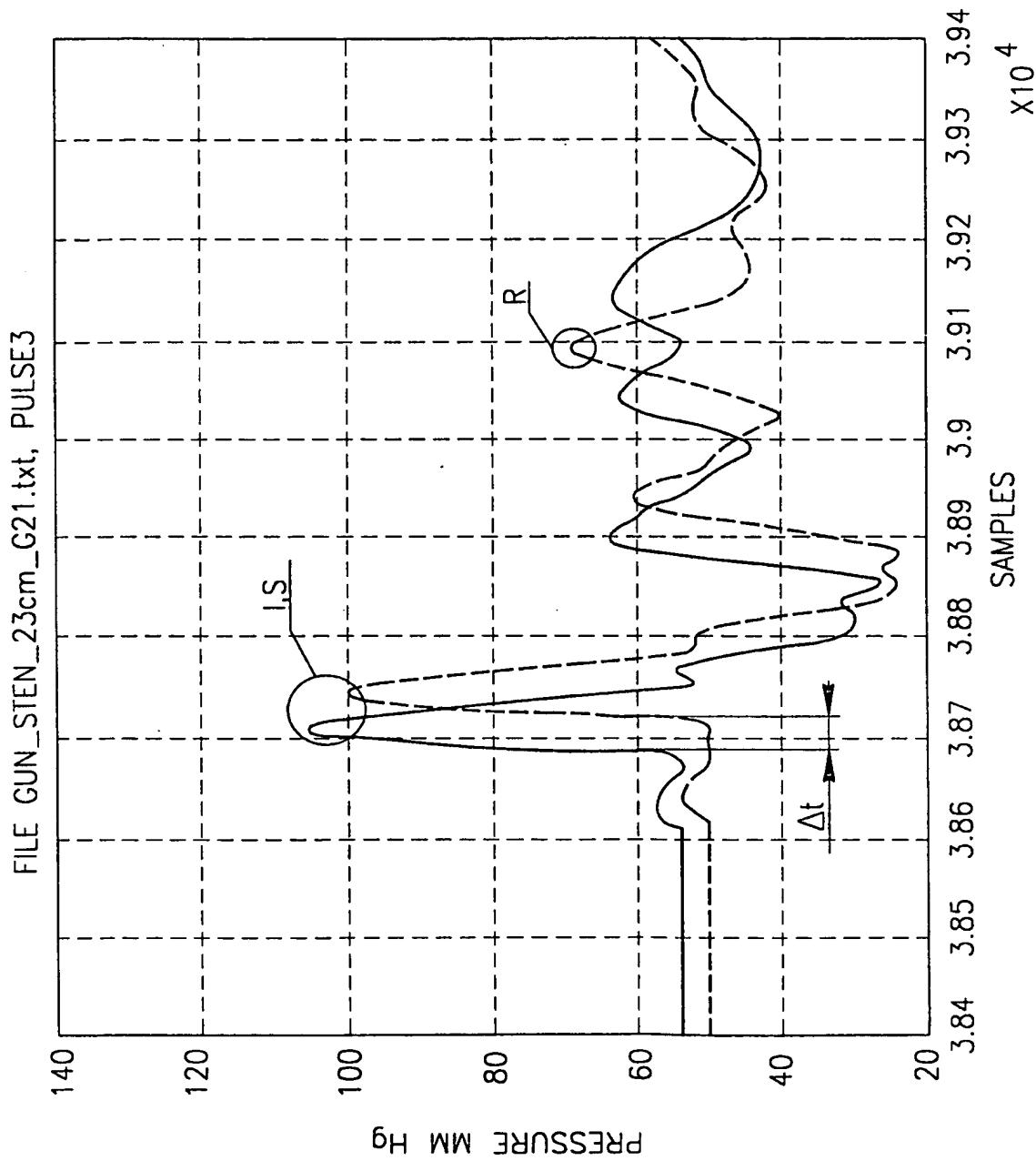


FIG.14

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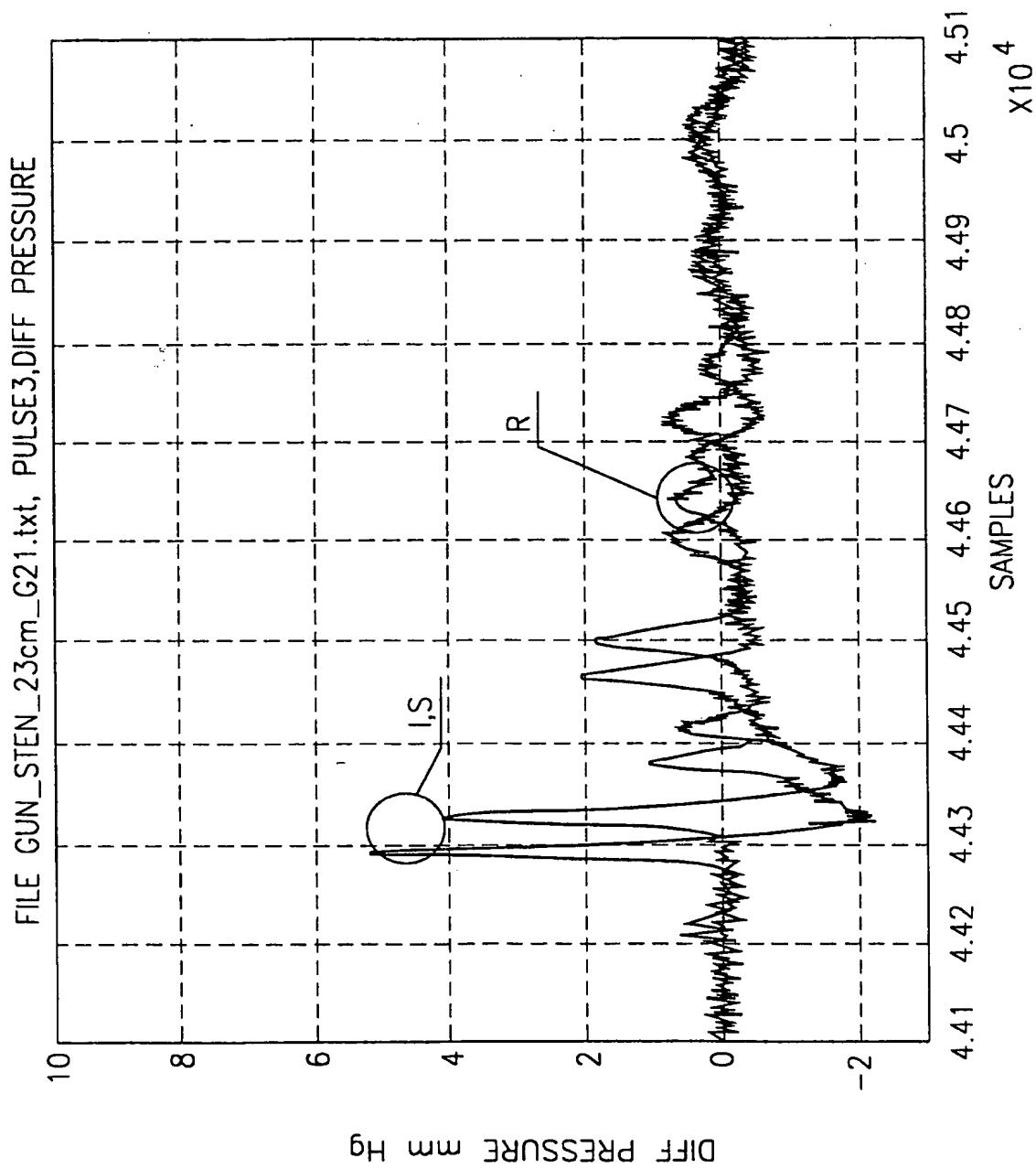


FIG.15

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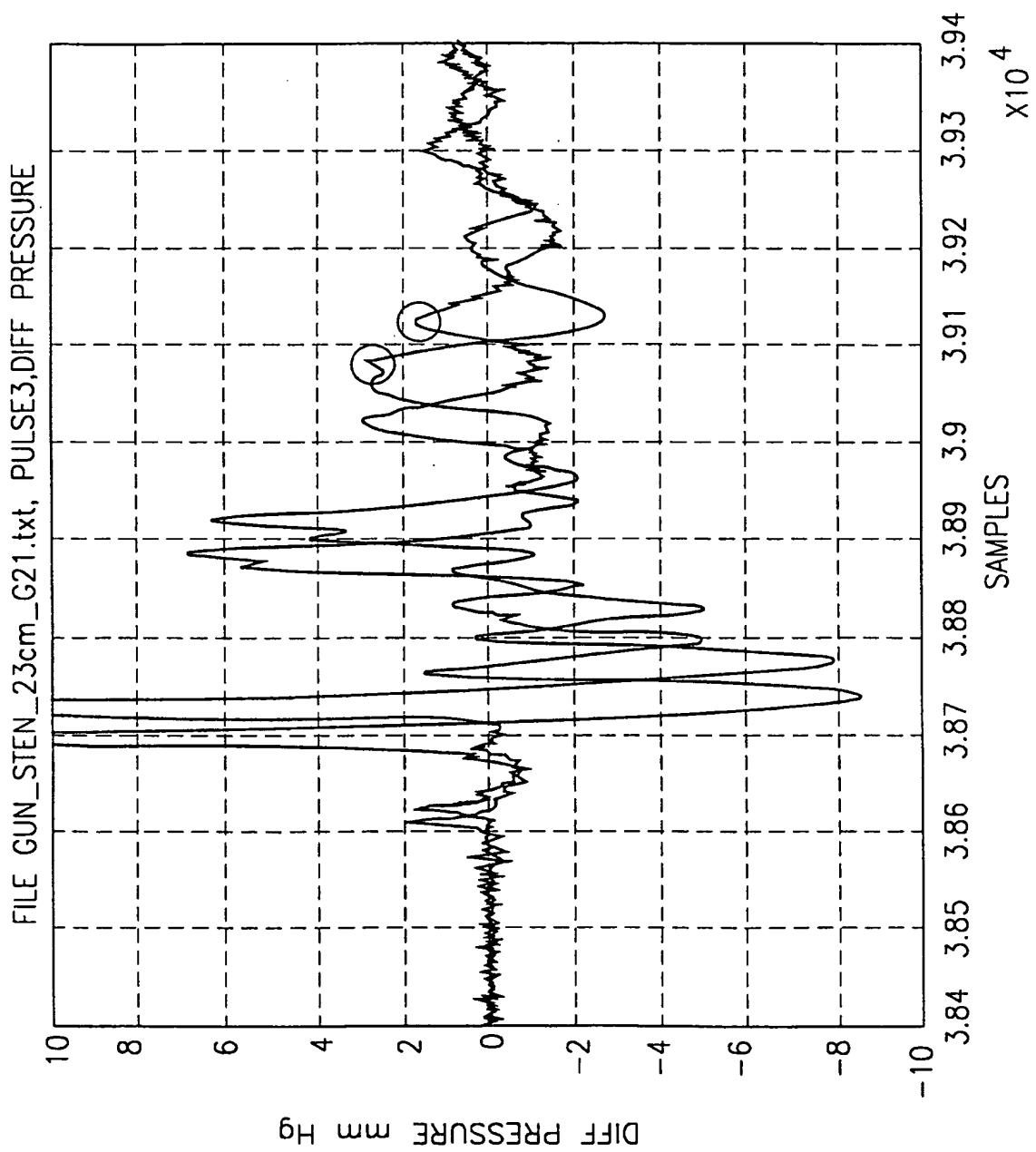
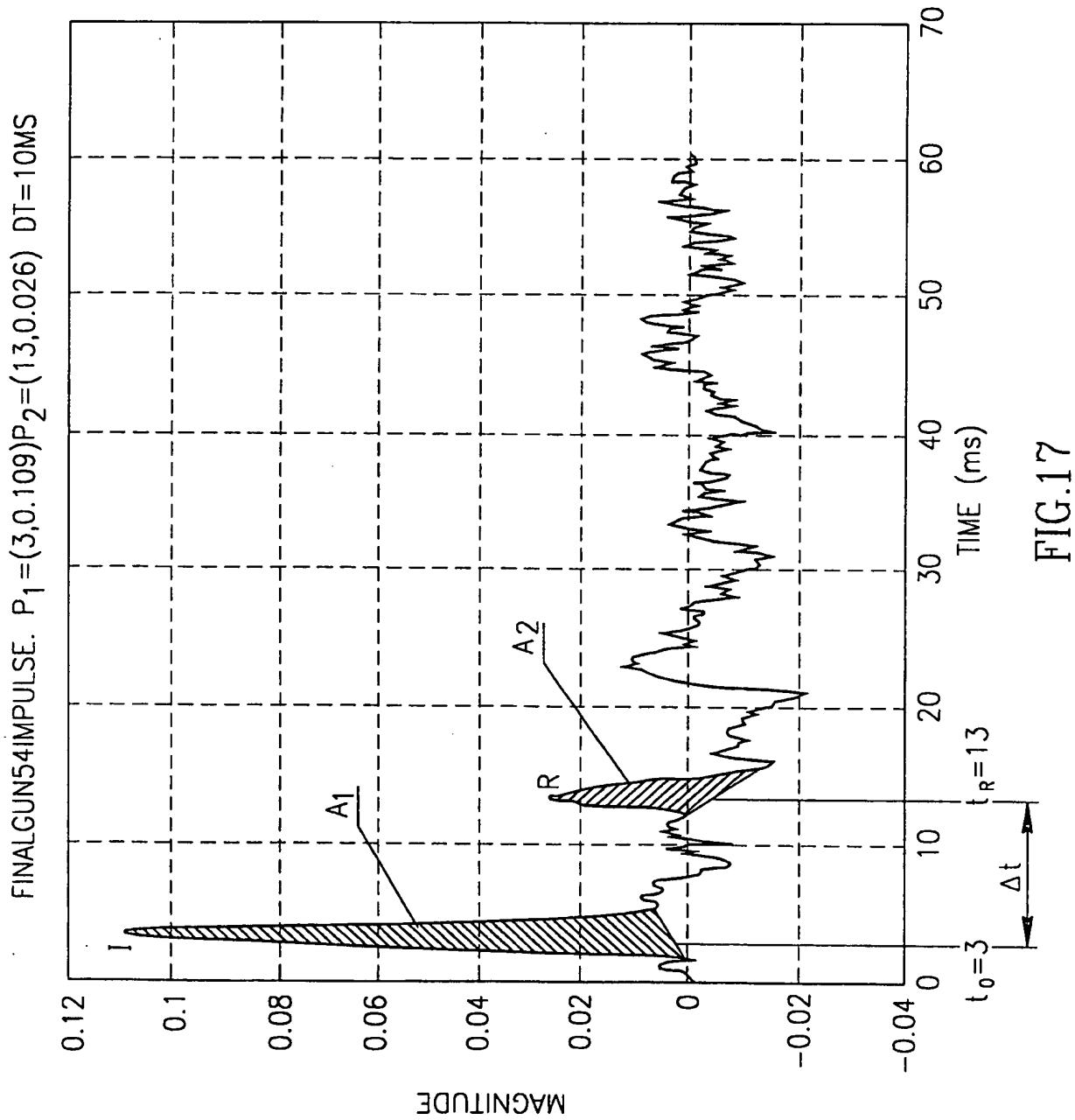


FIG. 16

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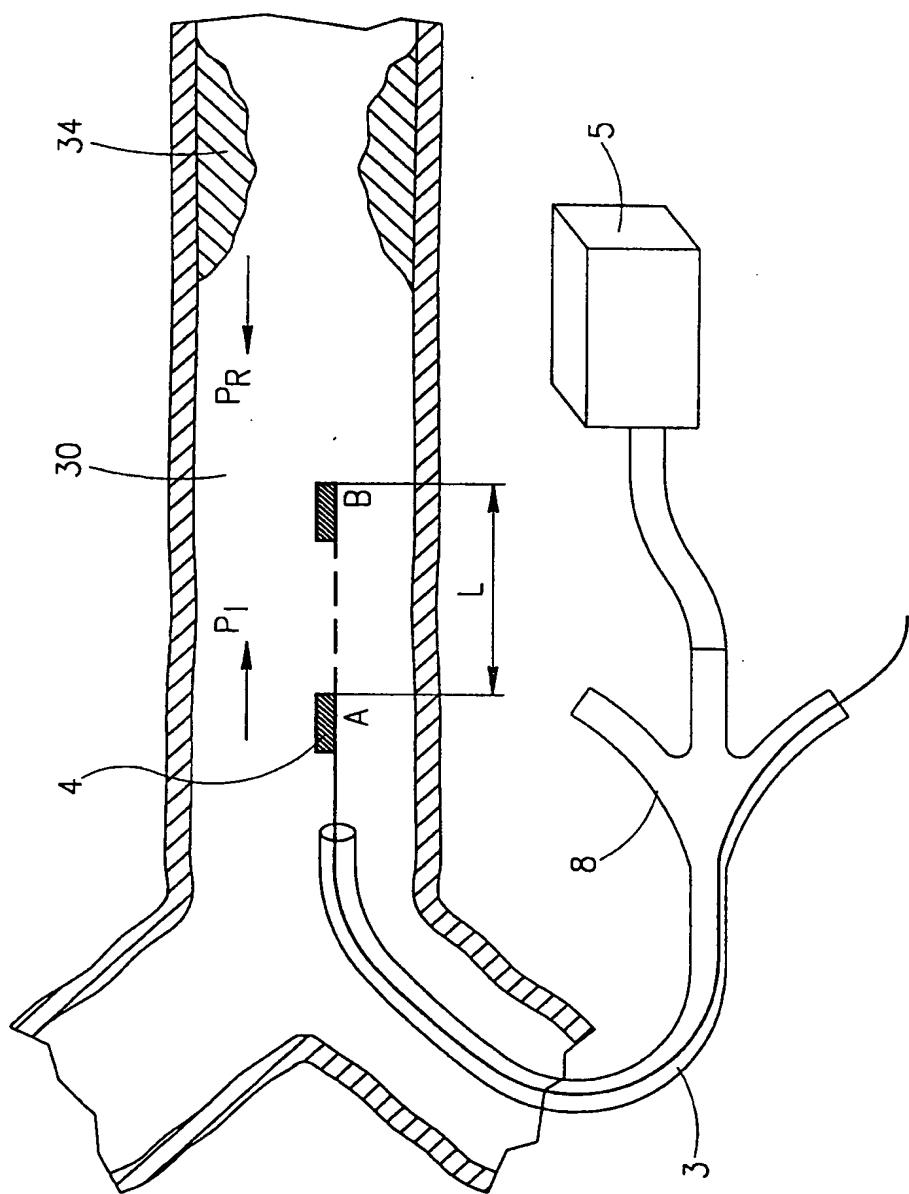


FIG.18

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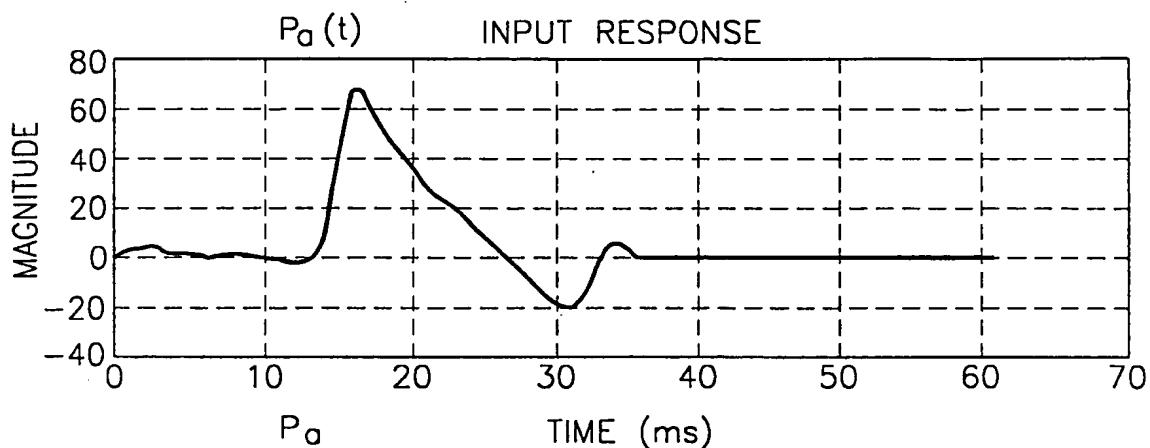


FIG.19A

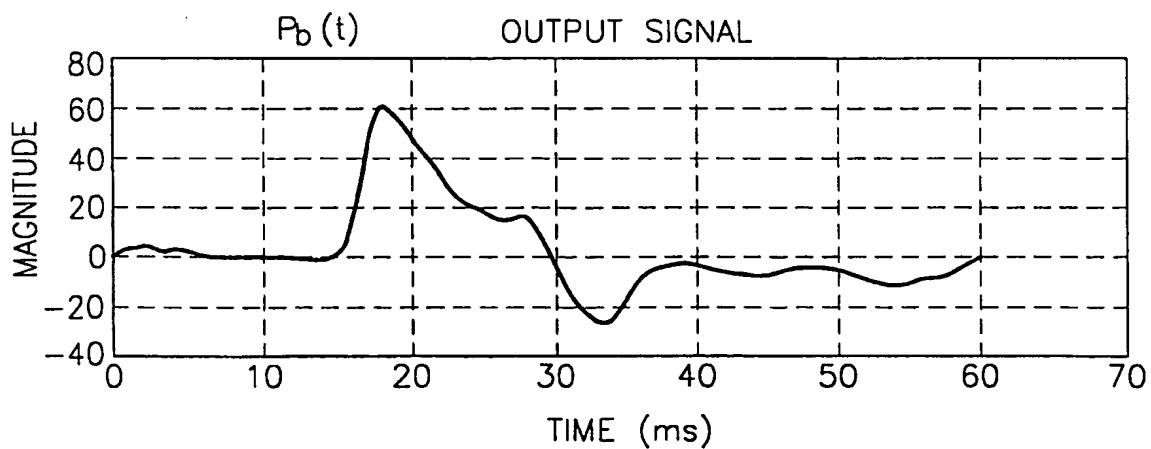


FIG.19B

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FINALGUN54IMPULSE RESPONSE.  $P_1=(3,0.109)$   $P_2=(13,0.026)$   $dT=10\text{ms}$

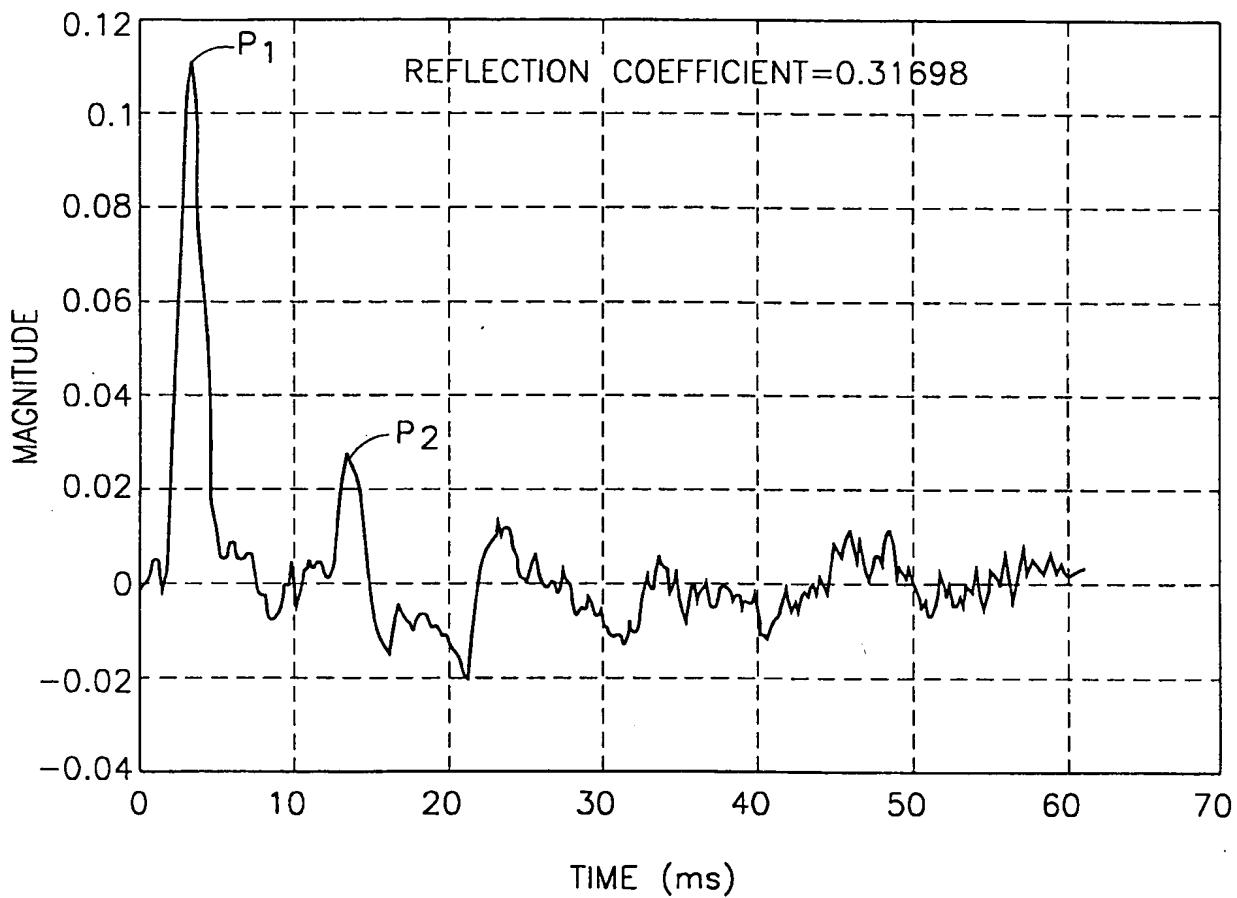


FIG.19C

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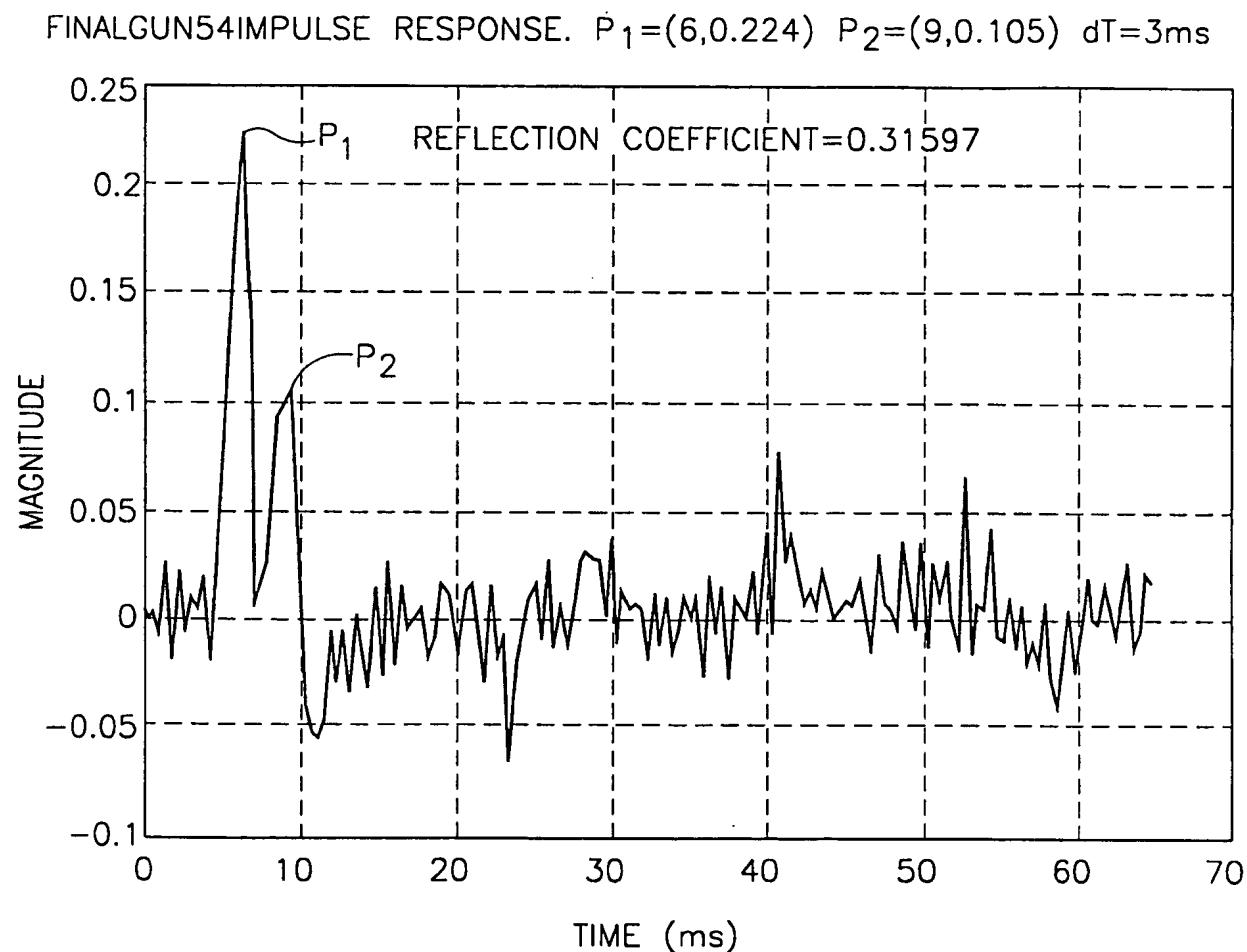


FIG.19d

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REF.COEFF,:0.34164 LOCATION: 0.0033718s

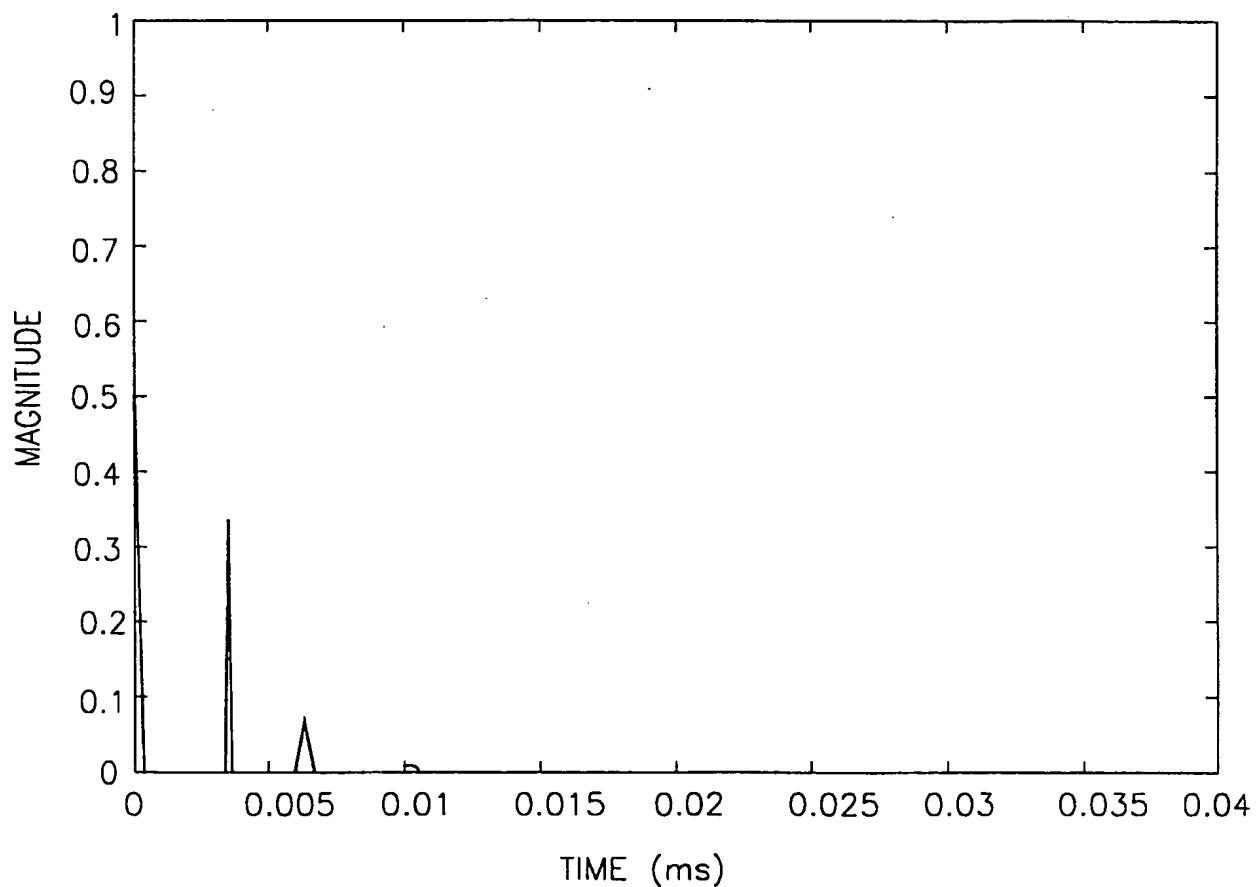


FIG.19E

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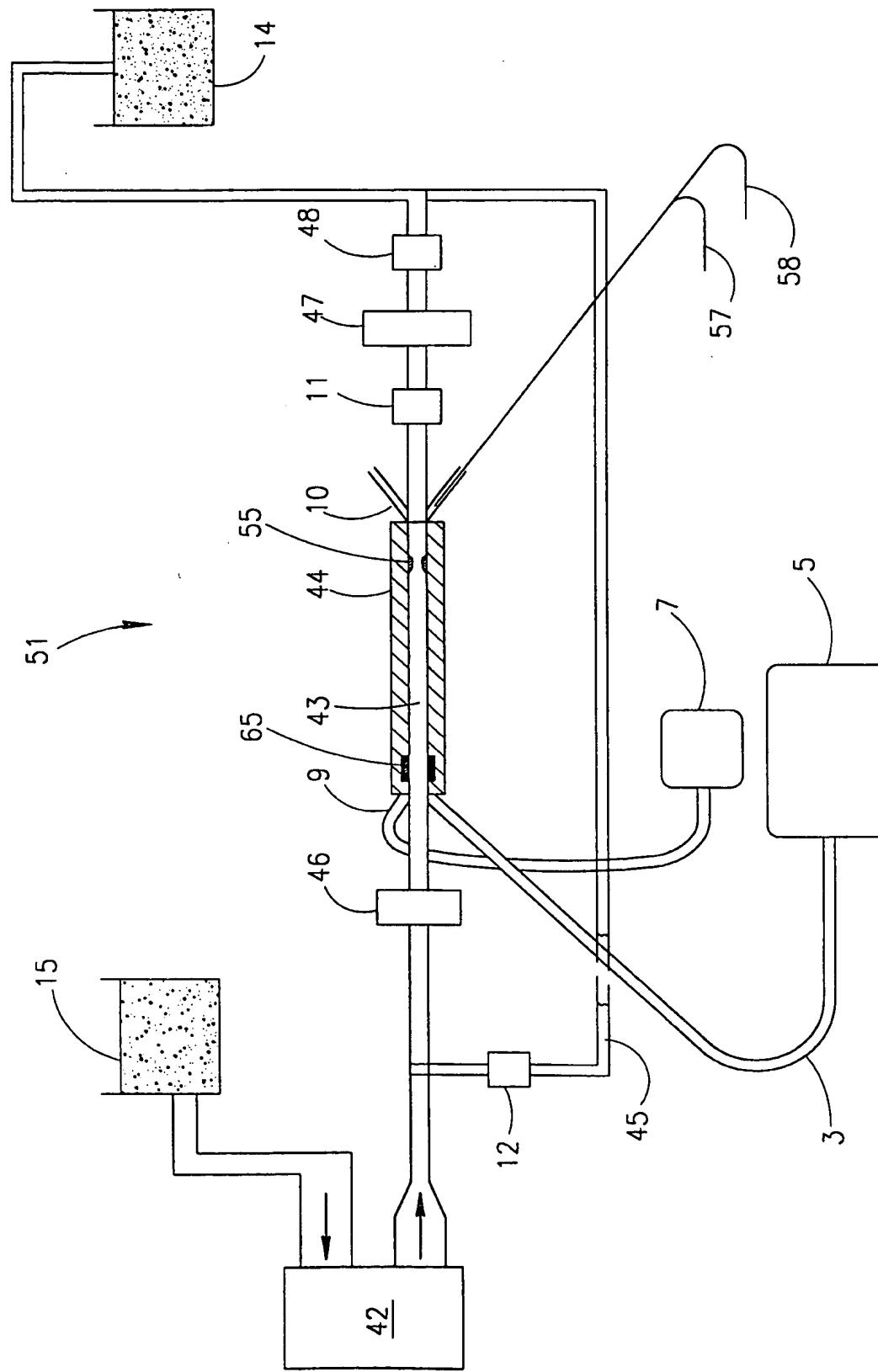


FIG. 20

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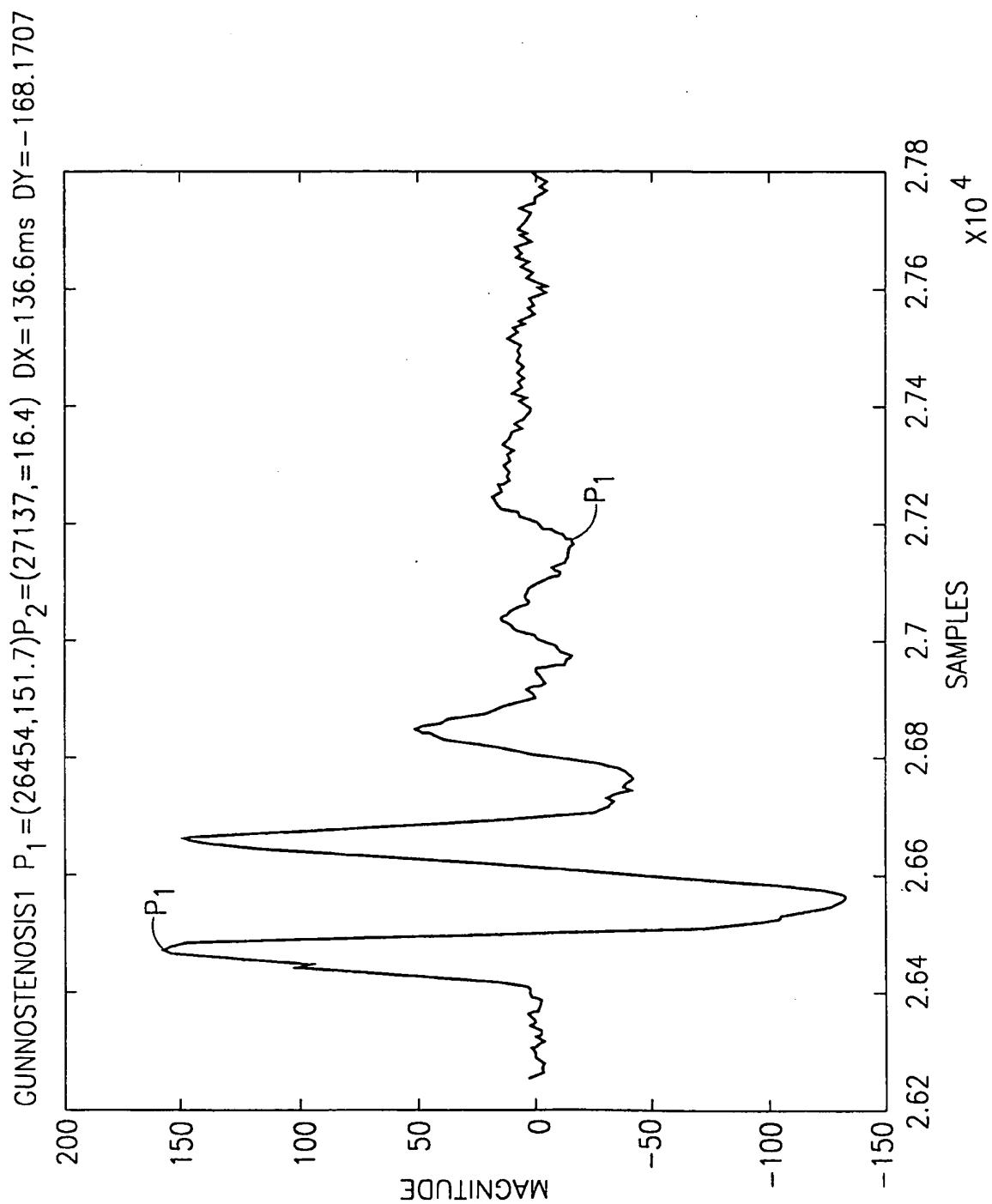


FIG.21

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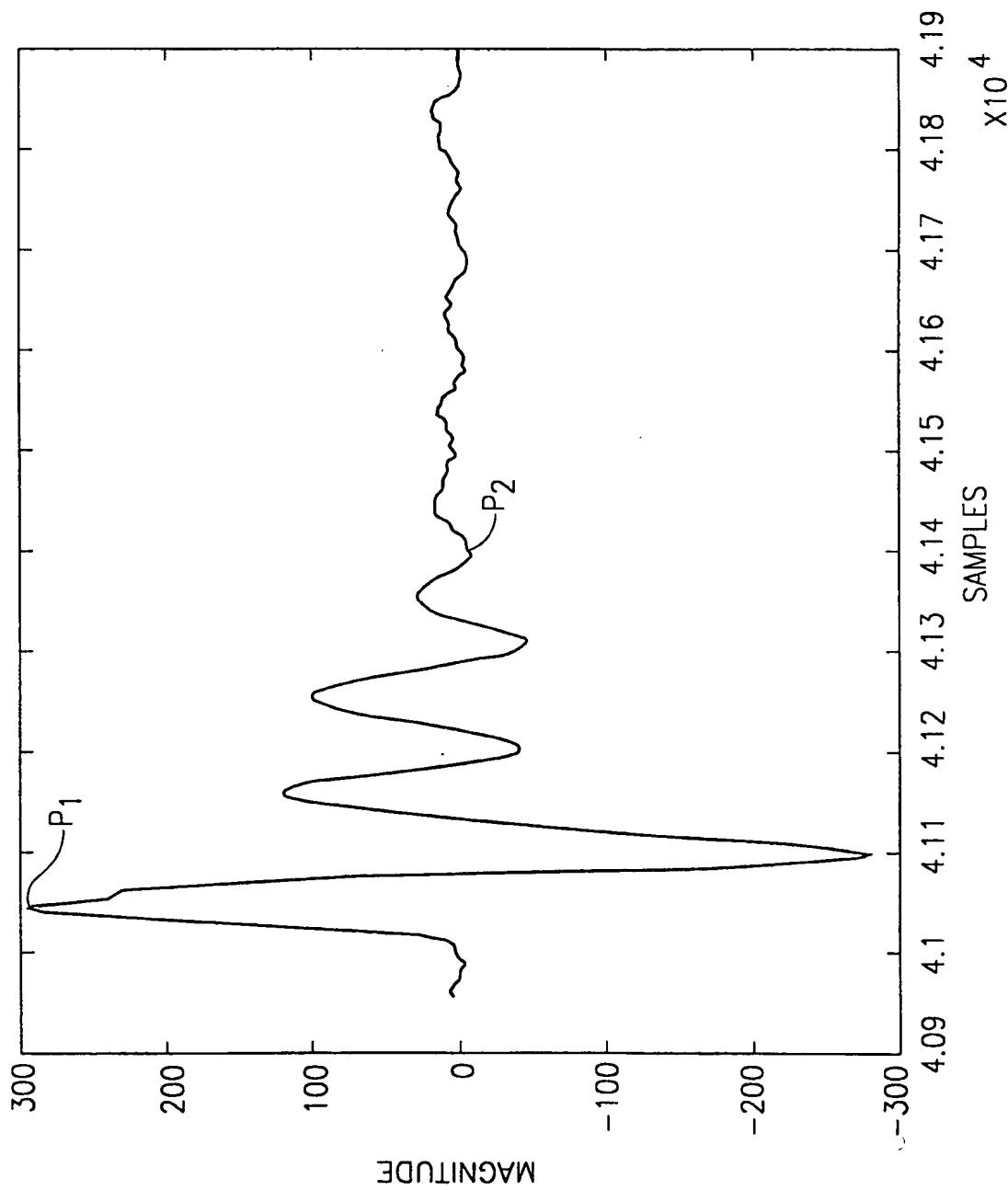
GUNNOSTENOSIS100d651.txt  $P_1 = (41030, 296.3)$   $P_2 = (41403, -16.8)$   $DX = 74.6\text{ms}$   $DY = -313.1707$ 

FIG.22

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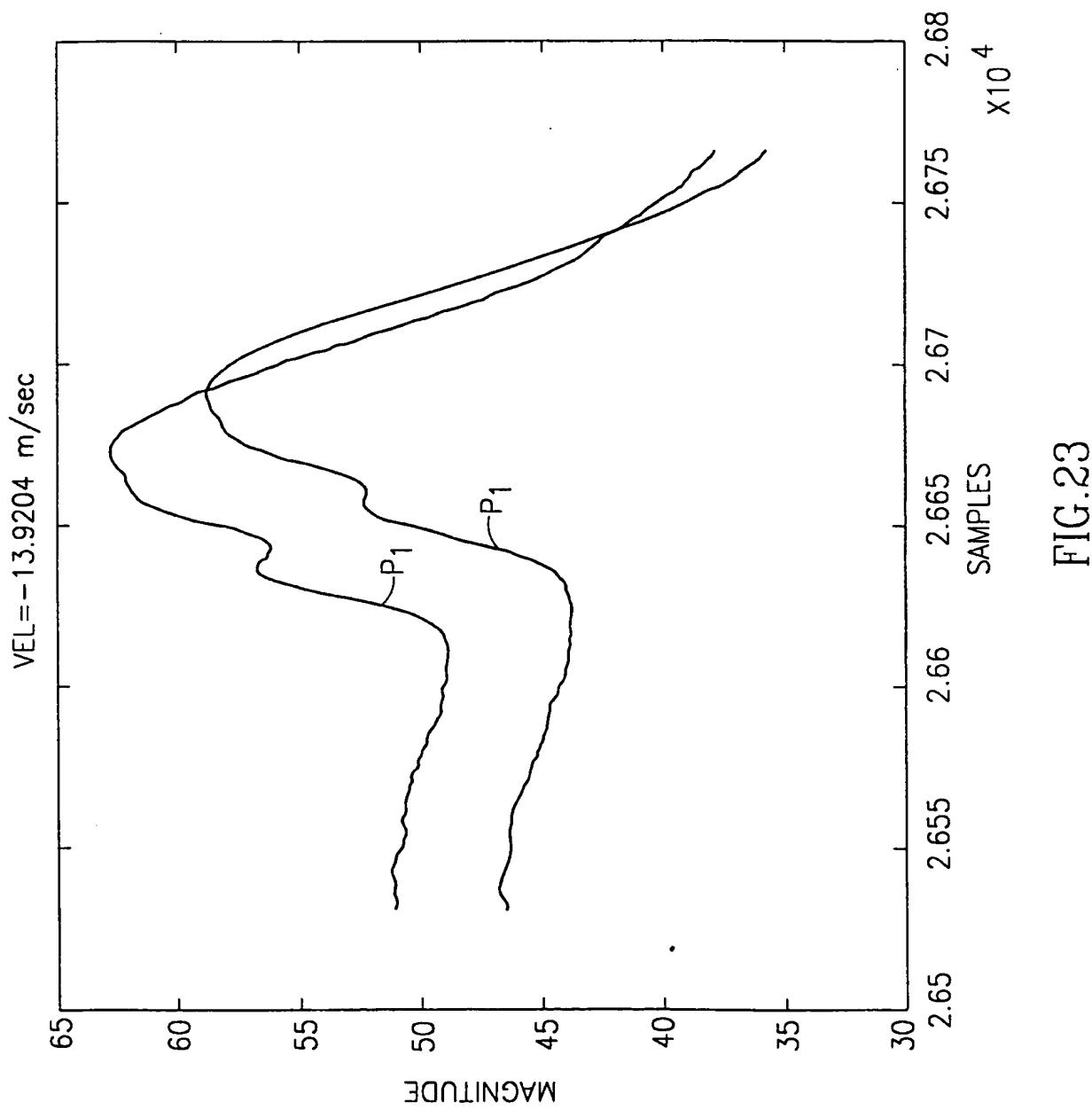


FIG. 23

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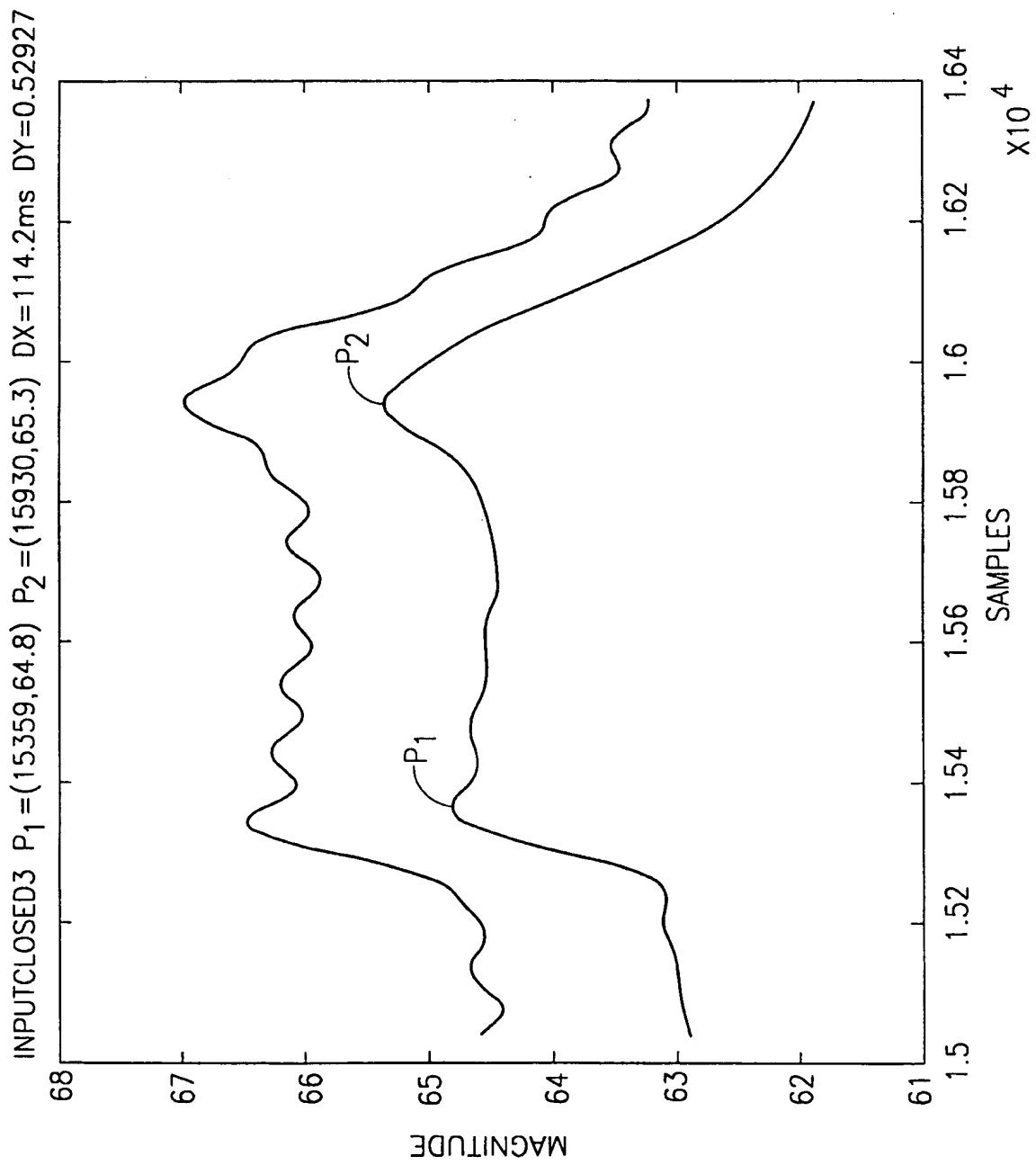


FIG.24

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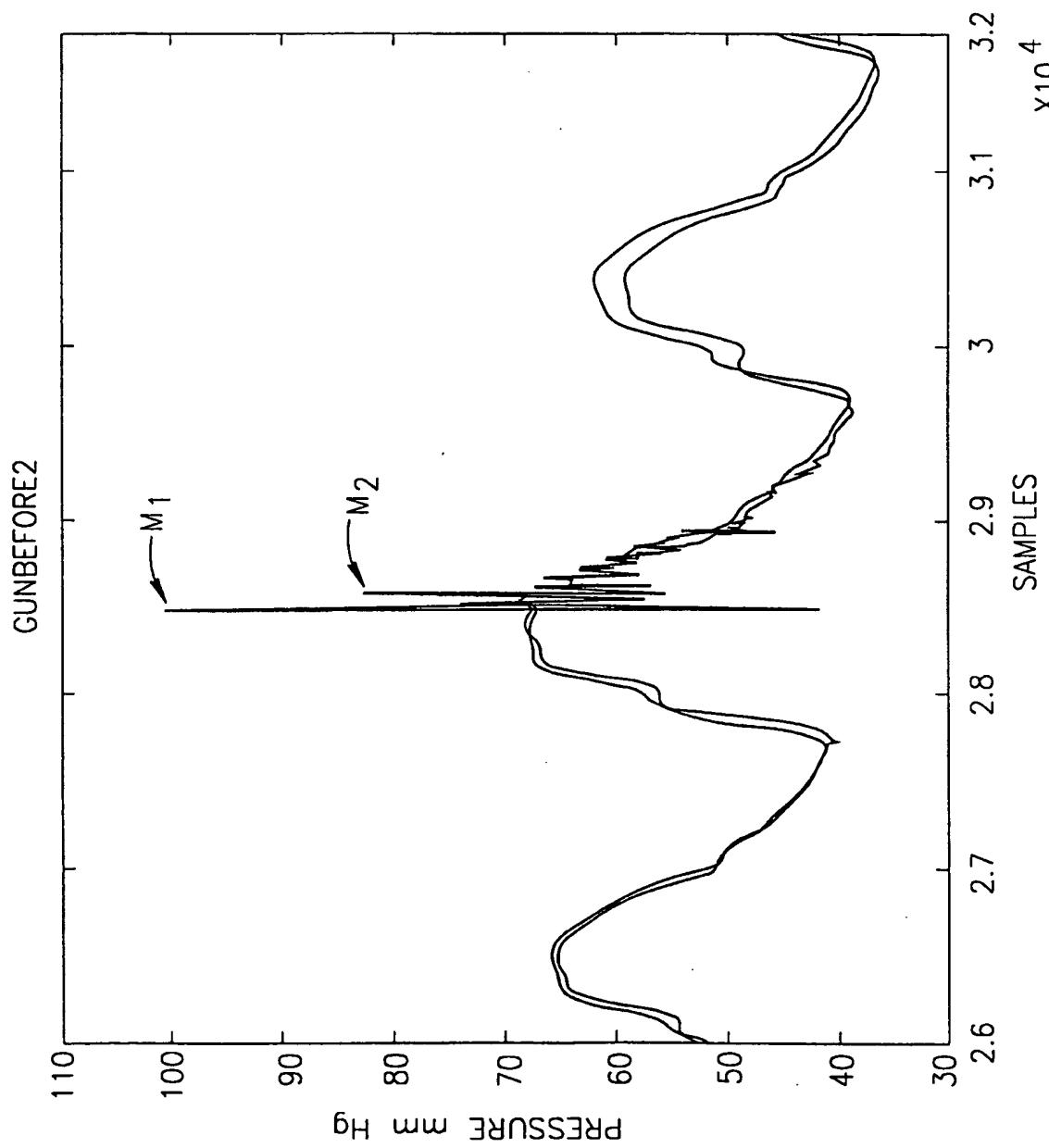


FIG. 25

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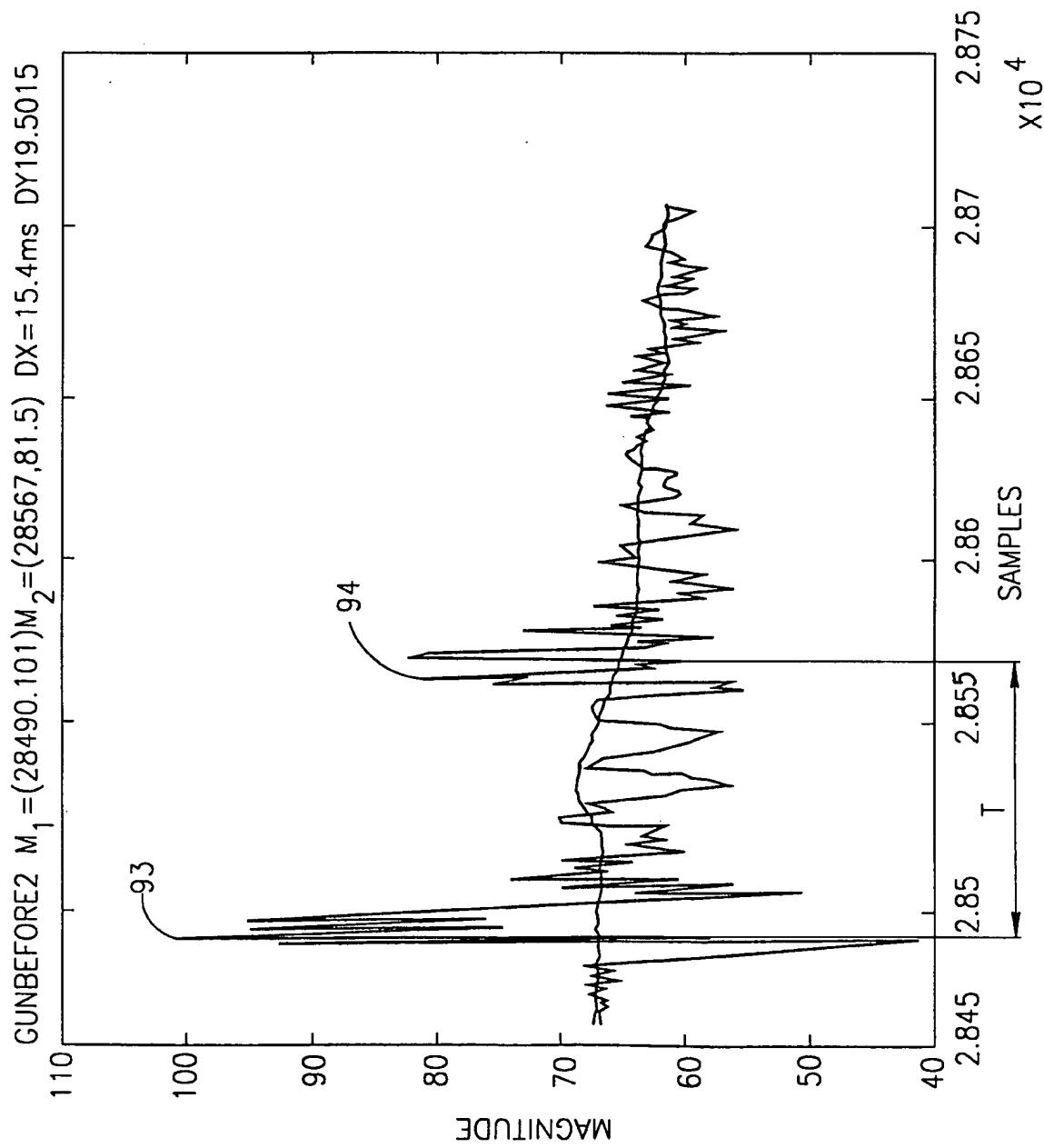


FIG. 26

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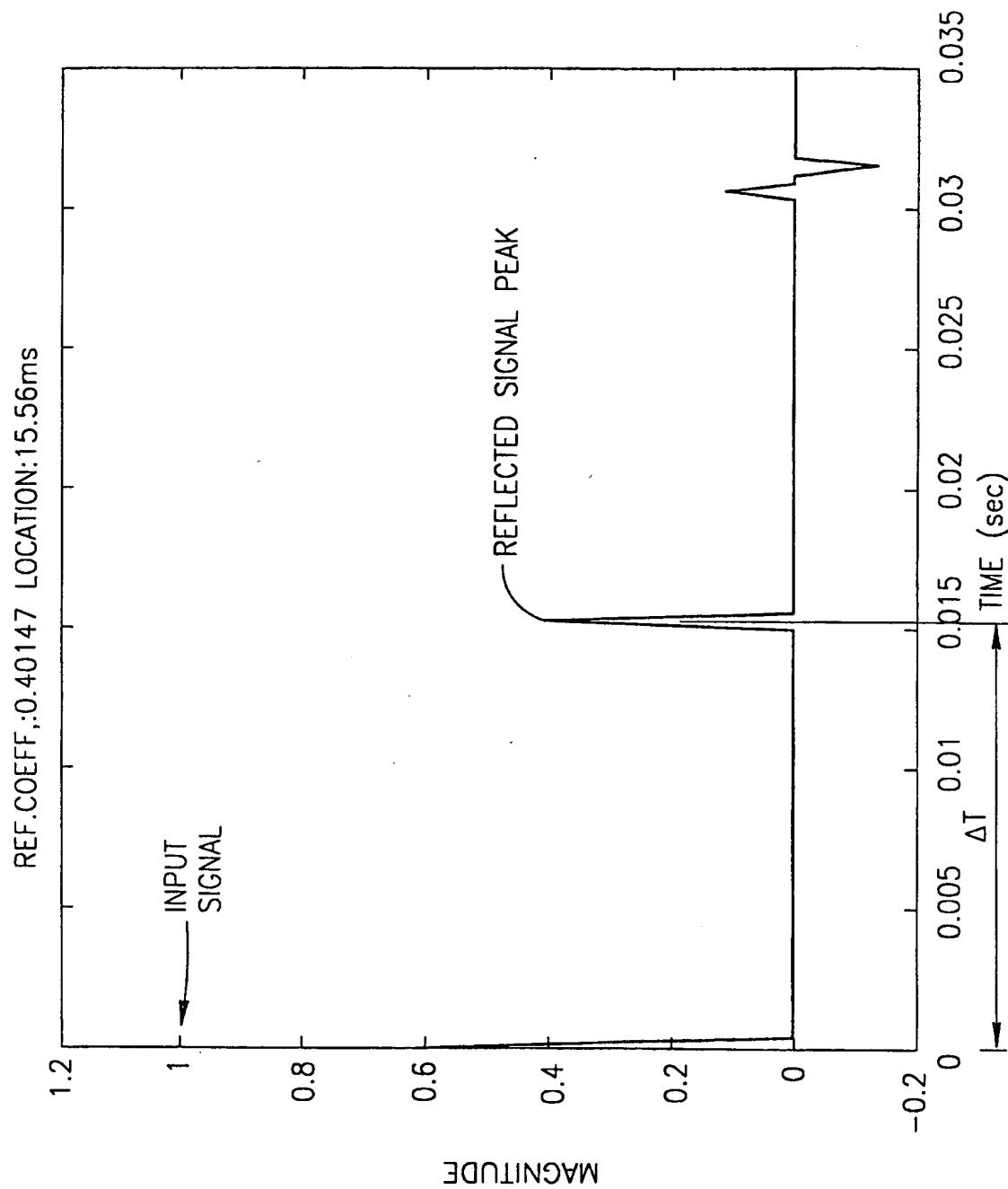


FIG. 27

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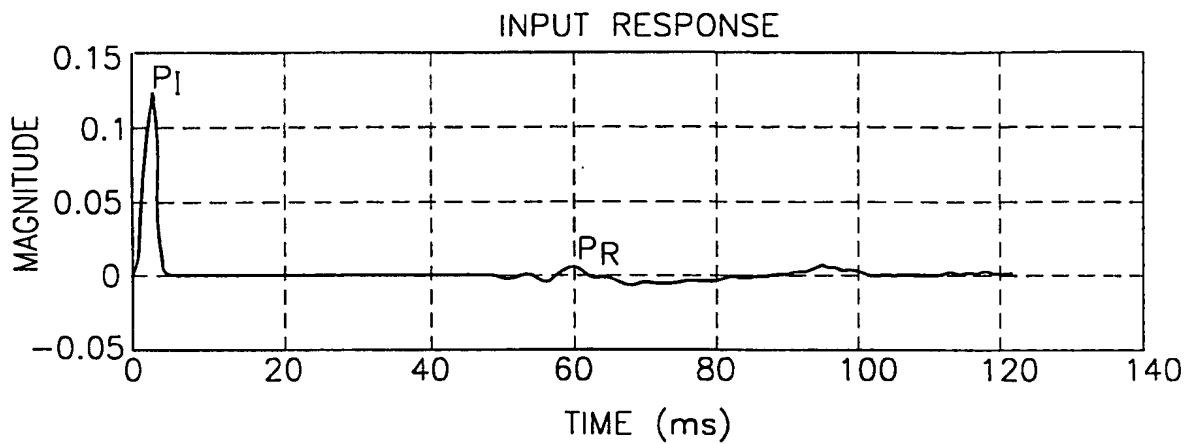


FIG.28A

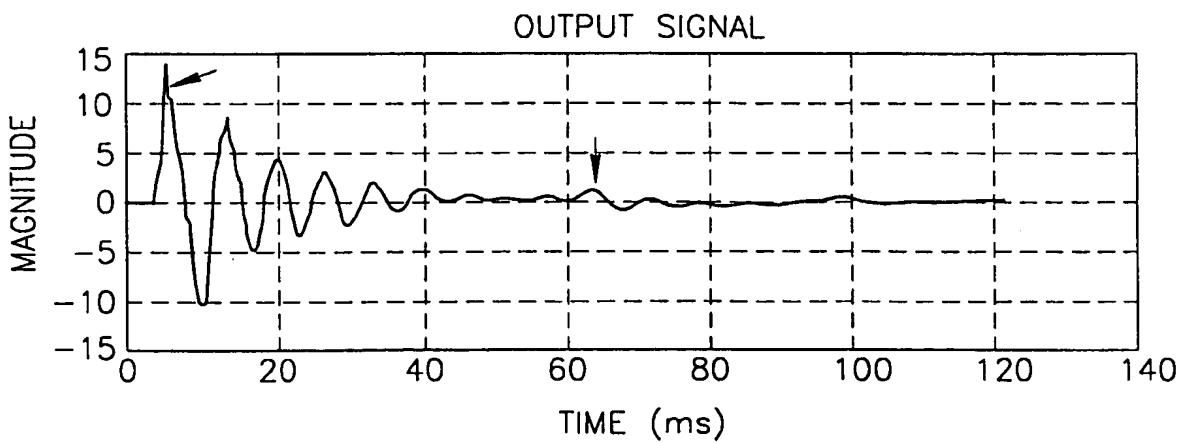
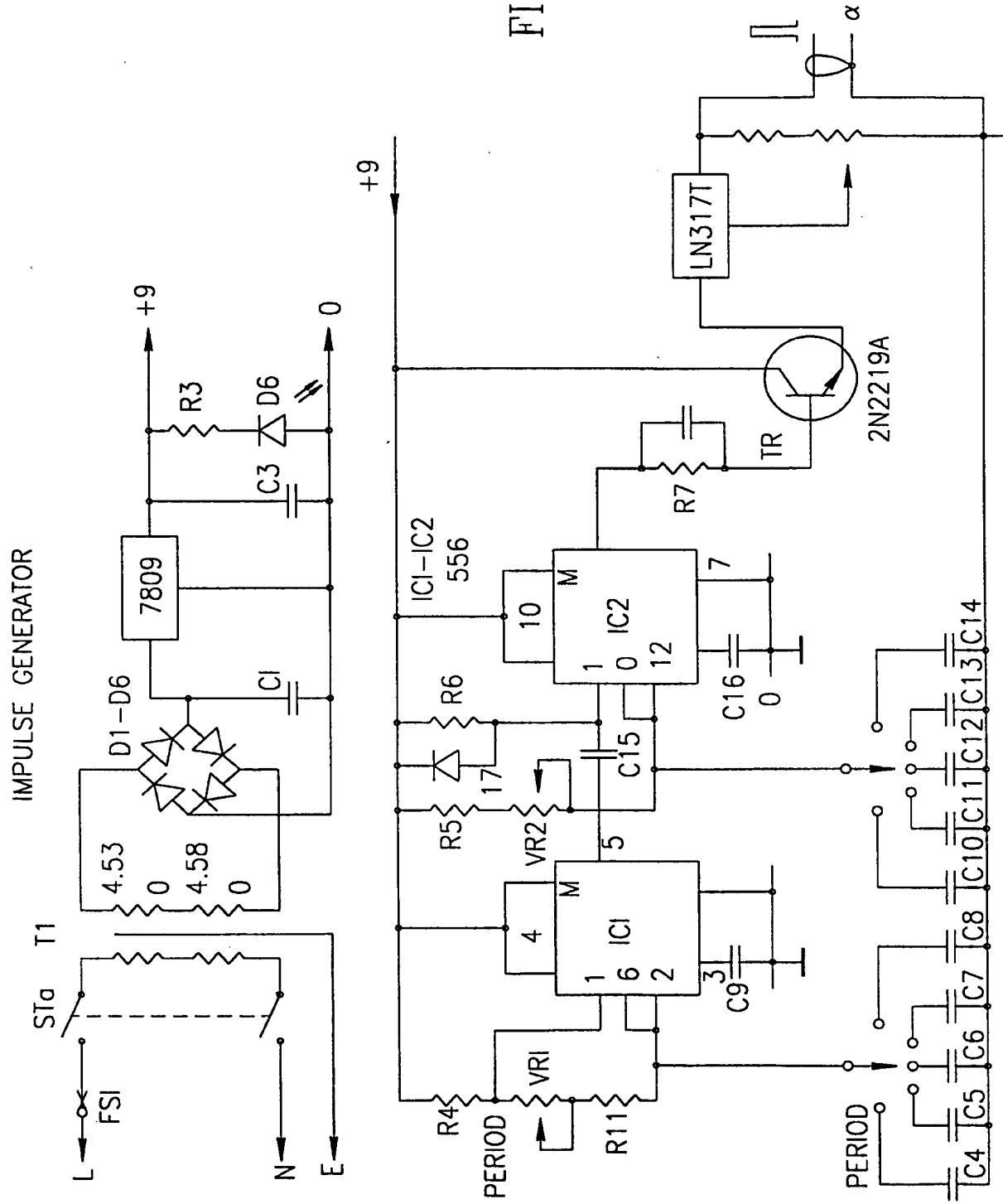


FIG.28B

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FIG.29A



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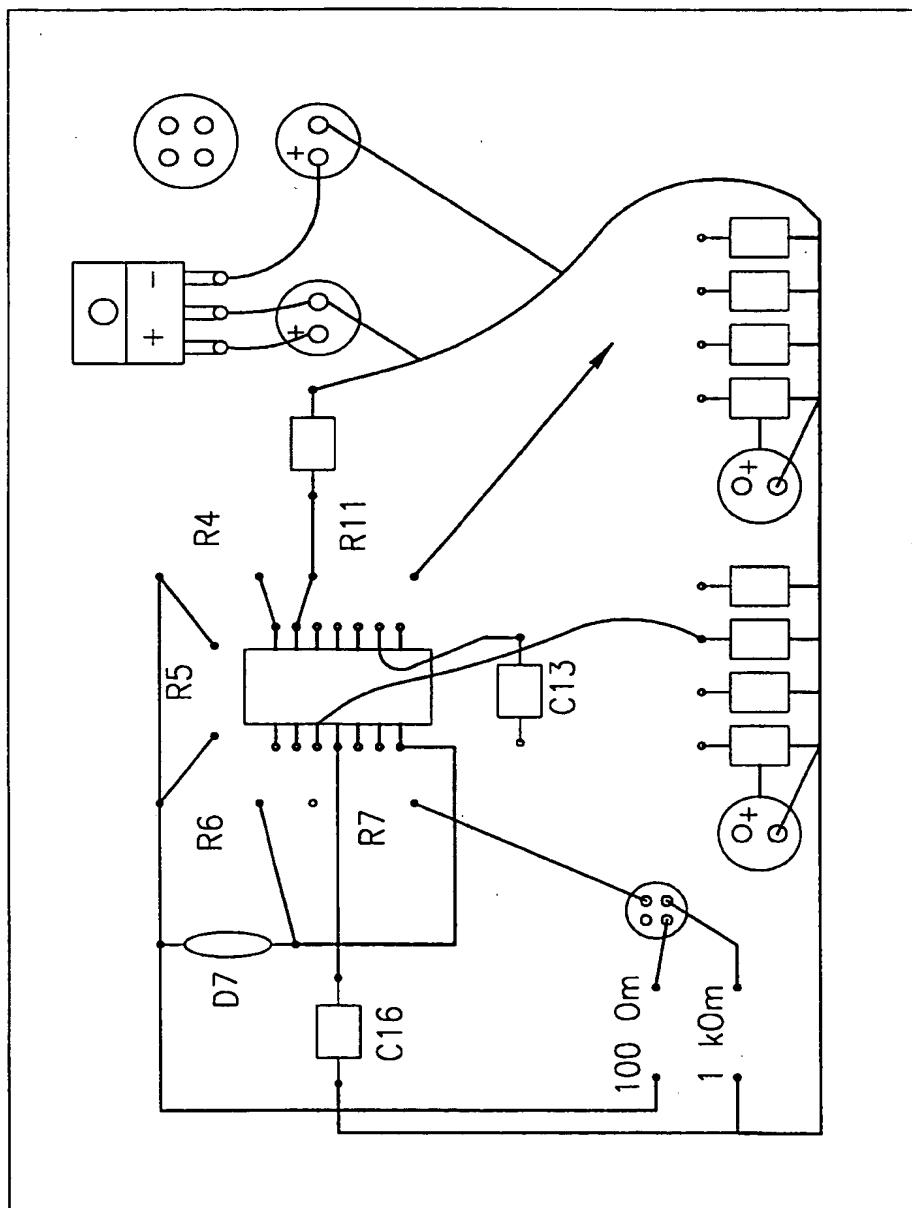


FIG.29B

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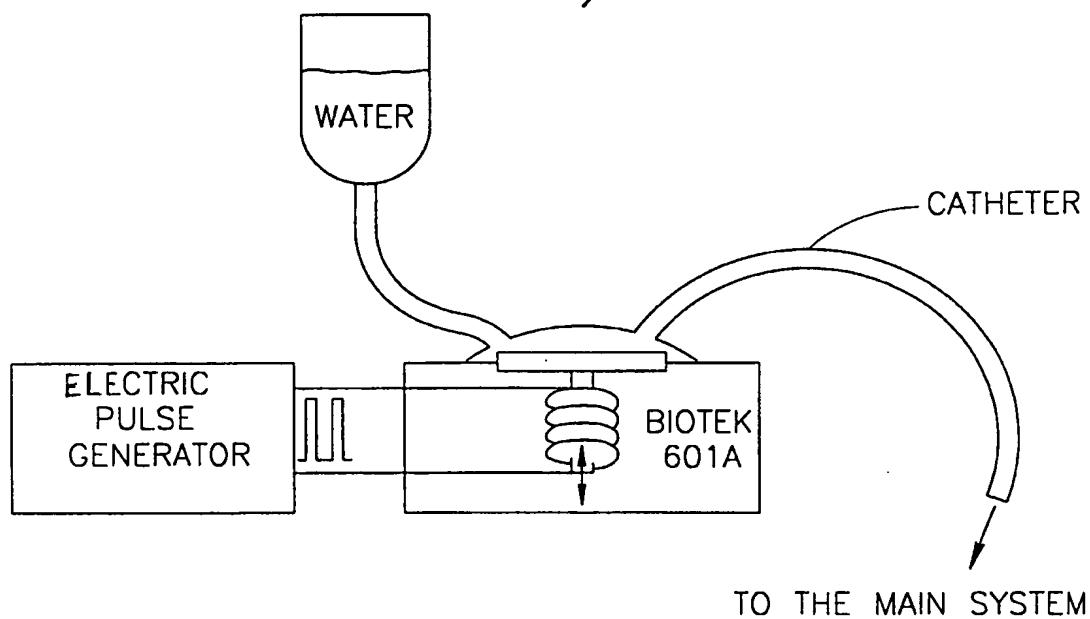


FIG.30

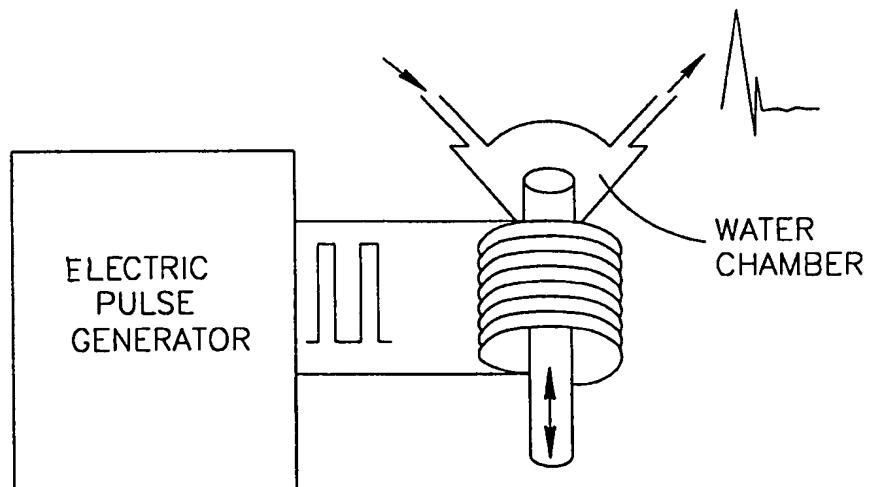


FIG.31

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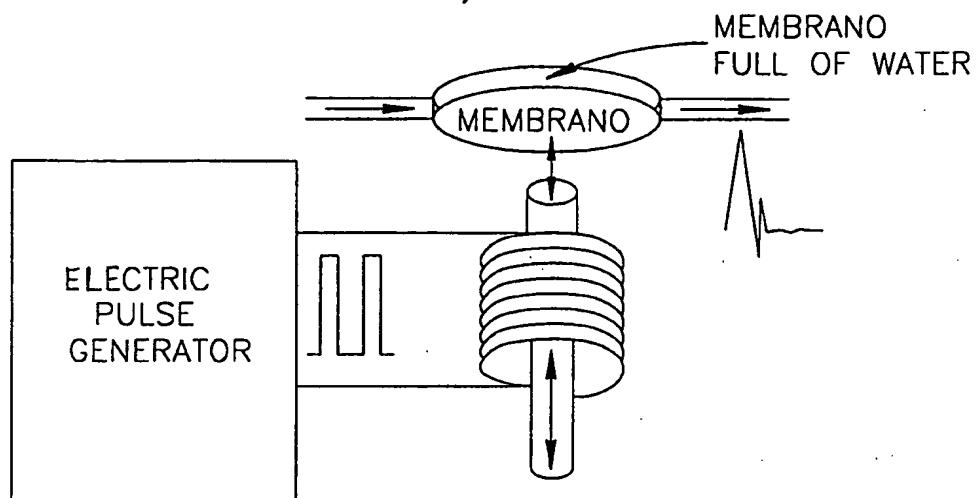


FIG.32

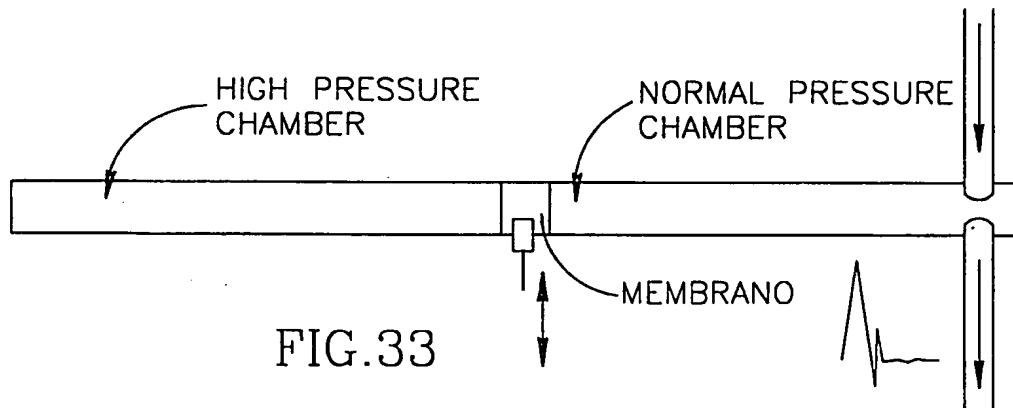


FIG.33

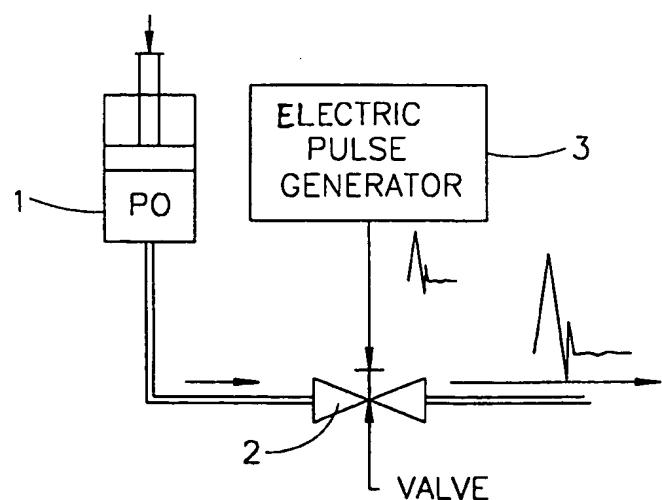


FIG.34

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EXITER DESCRIPTION

EXITER IS A DEVICE FOR THE EXCITATION OF THE PRESSURE WAVES INSIDE THE TUBE (CATHERETER). IT CONSISTS OF A HAMMER (95) AND CONICAL CHAMBER (96). LOW VOLTAGE IS APPLIED TO THE SOLENOID (NOT SHOWN) THAT PUSHES THE WEIGHT (HAMMER). THIS WEIGHT STROKES THE MEMBRANE (97) OF THE CONICAL CHAMBER THUS INITIATING A SHORT PRESSURE PULSE. THE OPENING OF THE CONE IS CONNECTED TO A CATHETER (98). IN THE INITIAL STATE THE CHAMBER AND THE CATHETER ARE FILLED WITH THE FLUID. THE MOVEMENT OF THE MEMBRANE IS ALLOWED ONLY IN ONE DIRECTION, SO ONLY POSITIVE PRESSURE PULSE IS PRODUCED. MEMBRANE CAME BACK TO THE INITIAL POSITION BY THE EFFECT OF RETURNING SPRING. DISPLACEMENT OF THE MEMBRANE AND PRESSURE WAVE GENERATION COULD BE ACHIEVED AS WELL BY USING AN ACTUATOR BASED ON PIEZOELEMENT OR OTHER DEVICE.

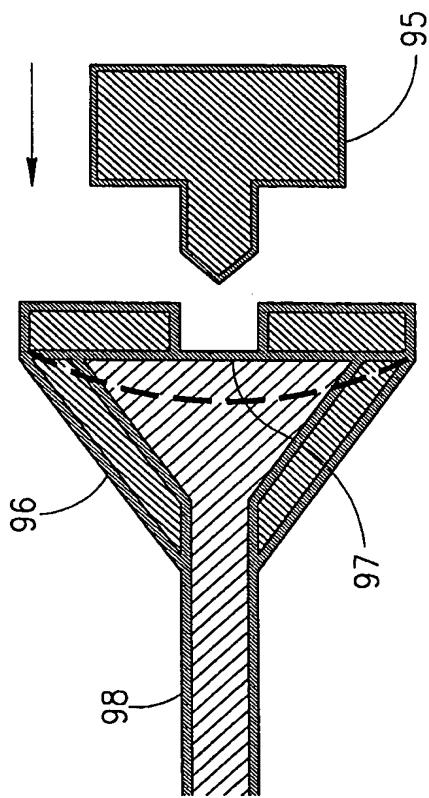


FIG. 35

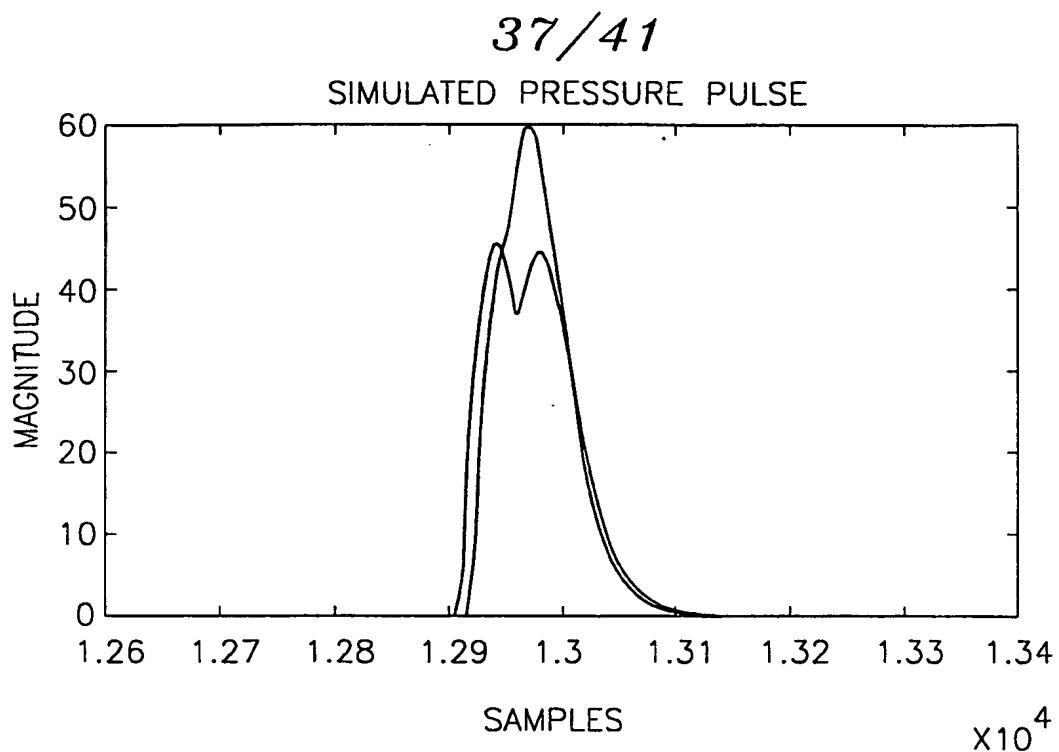


FIG.36

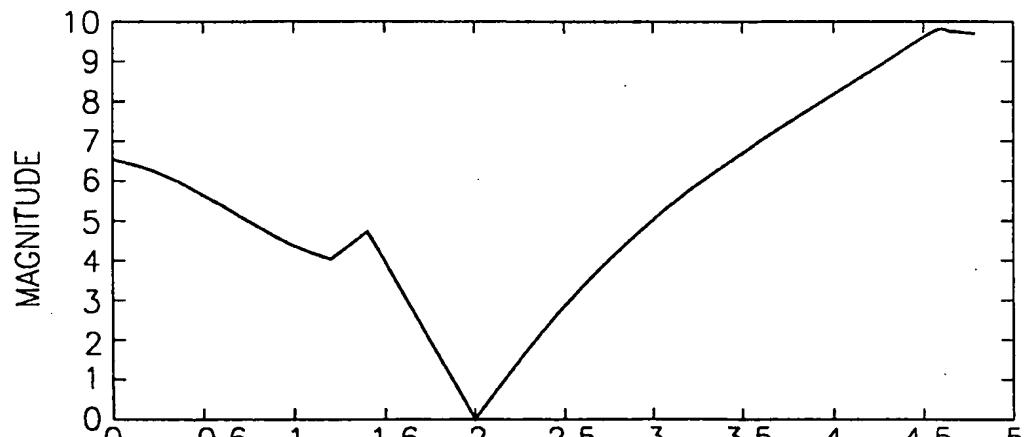


FIG.37

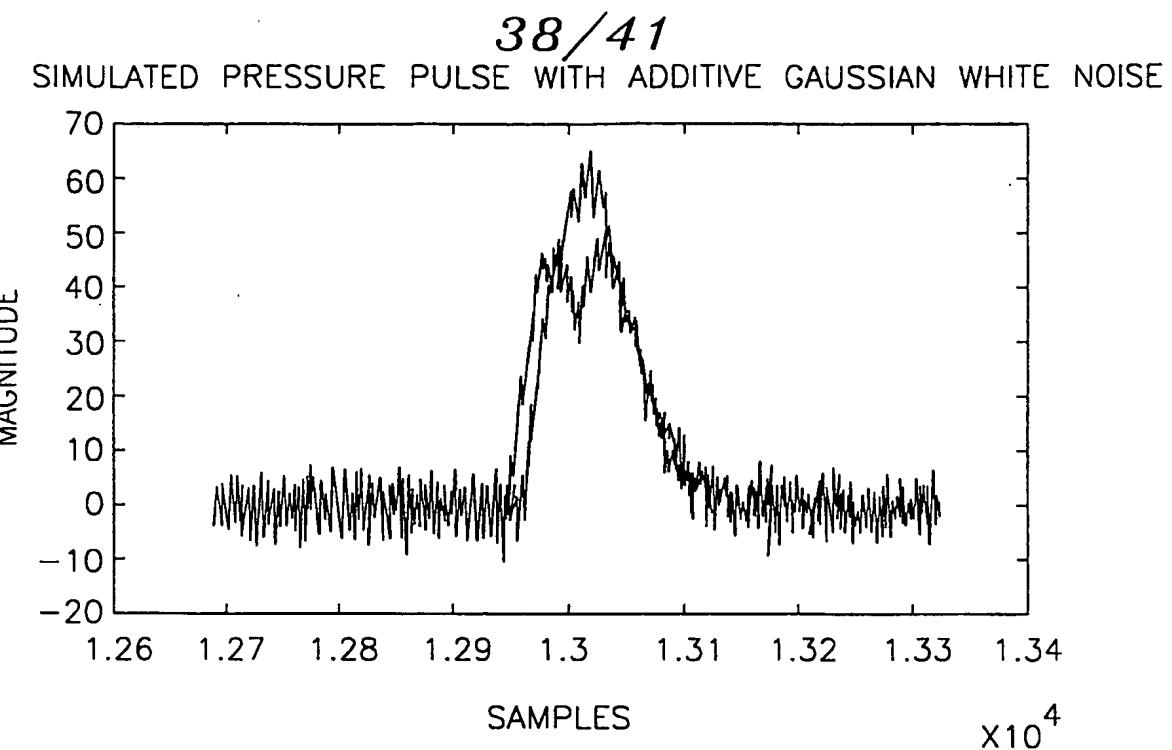


FIG.38

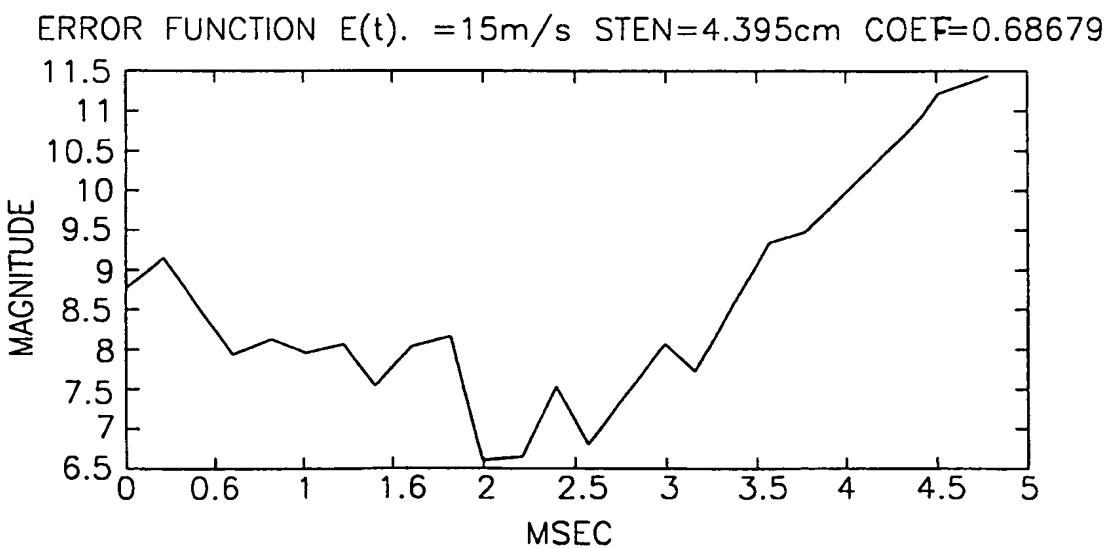


FIG.39

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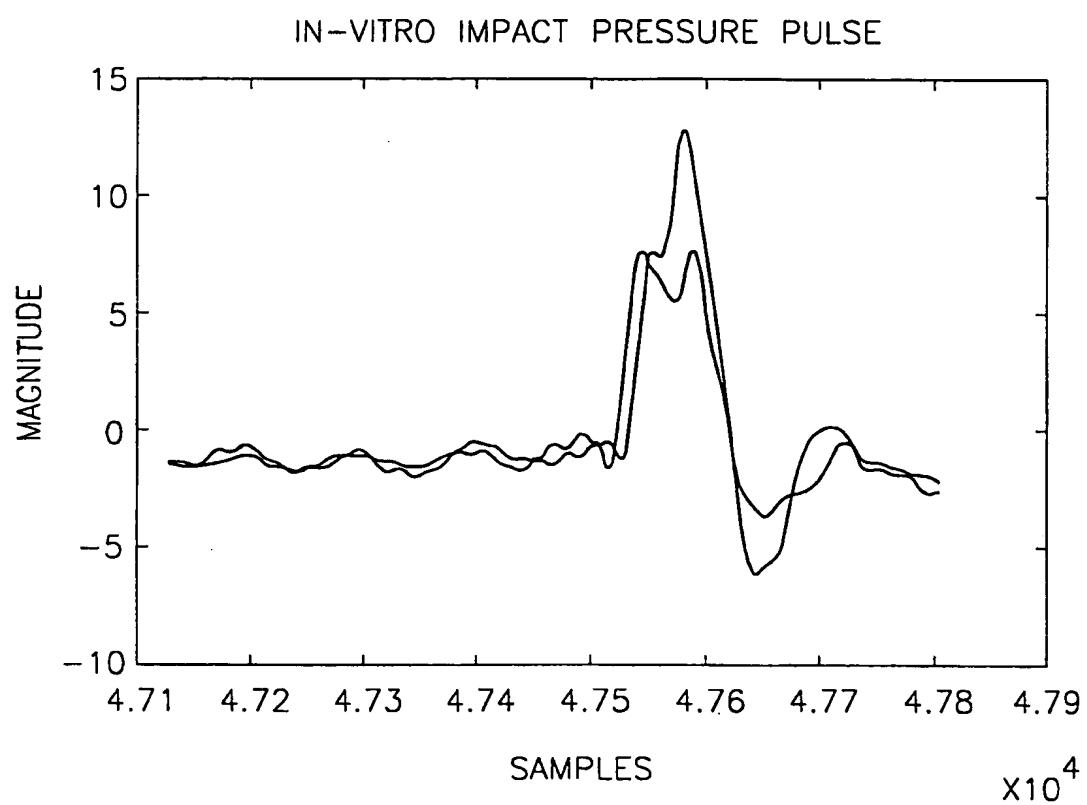


FIG. 40

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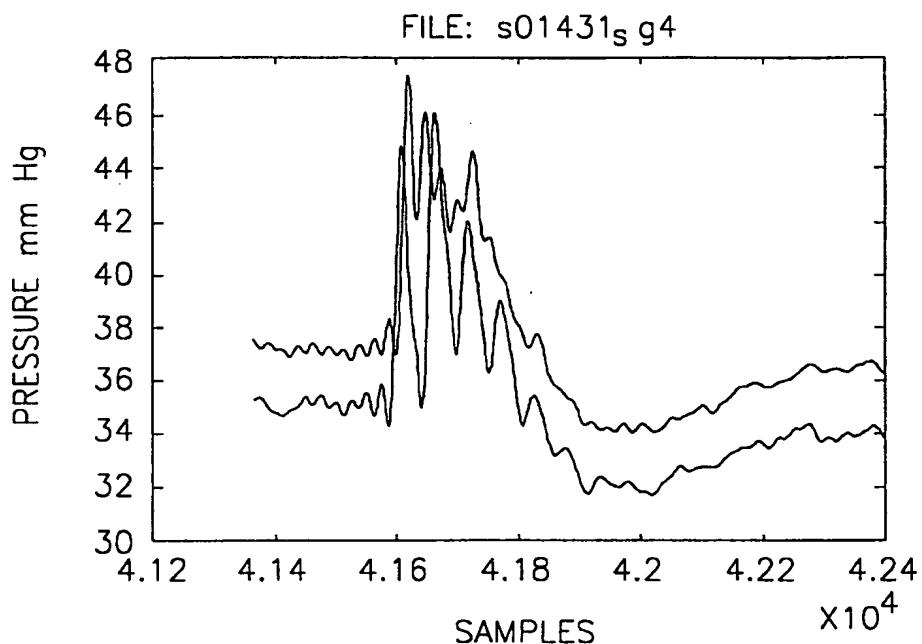


FIG.42

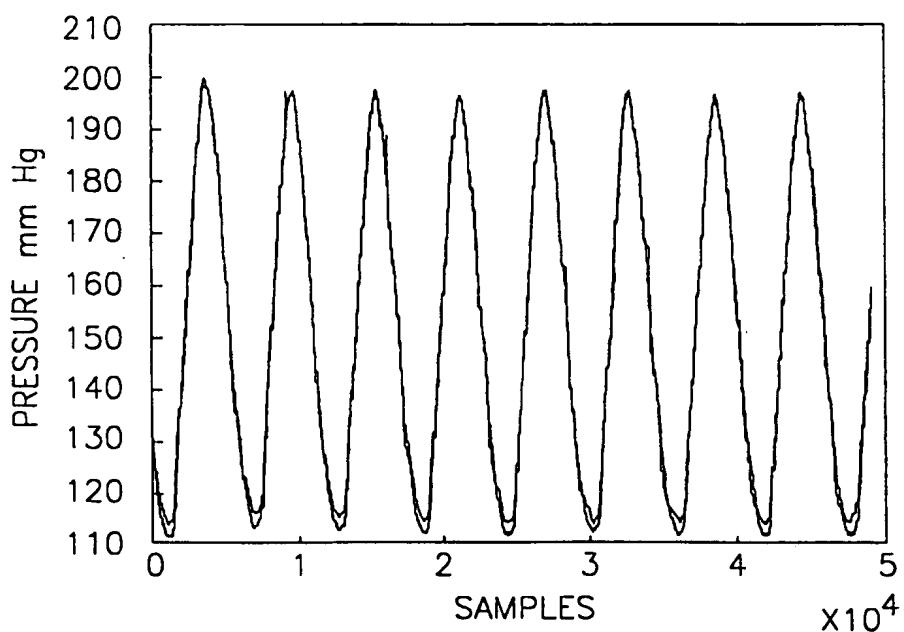


FIG.43

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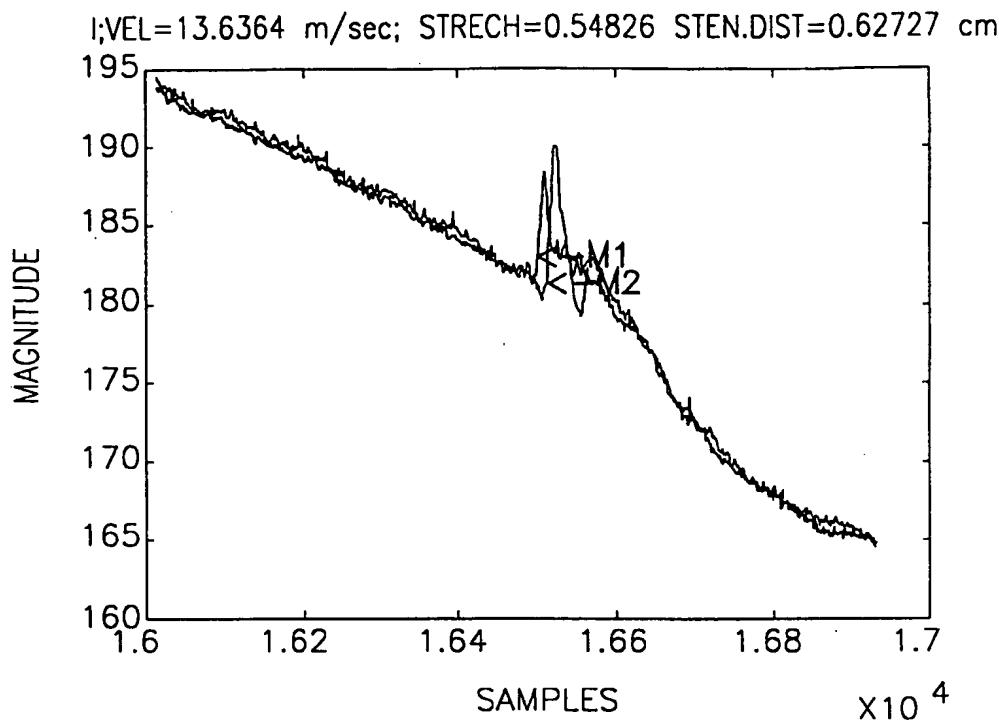


FIG.44

ERROR FUNCTION E(t). V=13.6364m/s STEN=4.3909cm COEF=0.62355

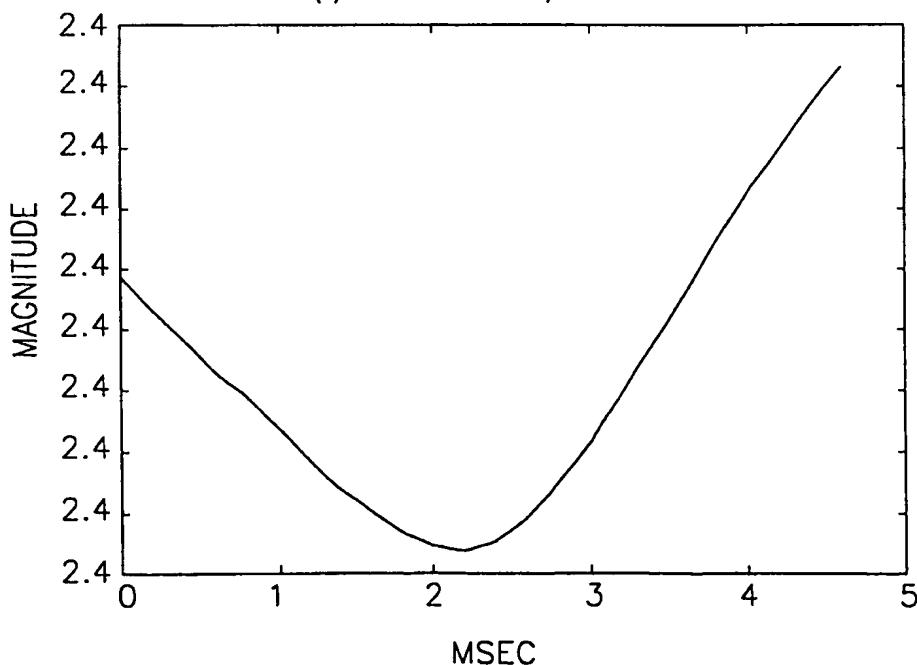


FIG.45  
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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IL99/00675

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61B 5/02  
US CL : 600/486

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 600/454, 481, 485, 486, 500, 504, 505

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim ▲
A	US 5,690,115 A (FELDMAN et al.) 25 November 1997, entire document.	1-85
A	US 5,343,867 A (SHANKAR) 06 September 1994, entire document.	1-85

Further documents are listed in the continuation of Box C.

See patent family annex.

Special categories of cited documents:			
*A*	document defining the general state of the art which is not considered to be of particular relevance	*T*	later document published after the international filing date or prior date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*B*	earlier document published on or after the international filing date	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*L*	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y*	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document combined with one or more other such documents, such combination being obvious to a person skilled in the art
*O*	document referring to an oral disclosure, use, exhibition or other means	*Z*	document member of the same patent family
*P*	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search  
12 MARCH 2000

Date of mailing of the international search report  
**12 APR 2000**

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